2015-04-06

Use of Opioids for Pain Management in Nursing Homes: A Dissertation

Camilla B. Pimentel

University of Massachusetts Medical School

USE OF OPIOIDS FOR PAIN MANAGEMENT IN NURSING HOMES

A Dissertation Presented

By

CAMILLA BENEDICTO PIMENTEL

Submitted to the Faculty of the

University of Massachusetts Graduate School of Biomedical Sciences, Worcester

in partial fulfillment of the requirements for the degree of

DOCTOR OF PHILOSOPHY

April 6, 2015

CLINICAL AND POPULATION HEALTH RESEARCH

USE OF OPIOIDS FOR PAIN MANAGEMENT IN NURSING HOMES

A Dissertation Presented

By

Camilla Benedicto Pimentel

The signatures of the Dissertation Defense Committee signify
completion and approval as to style and content of the Dissertation

Kate L. Lapane, Ph.D., Thesis Advisor

Robert J. Goldberg, Ph.D., Member of Committee

Jerry H. Gurwitz, M.D., Member of Committee

Beatriz Korc-Grodzicki, M.D., Ph.D., Member of Committee

Allison B. Rosen, M.D., M.P.H., Sc.D., Member of Committee

The signature of the Chair of the Committee signifies that the written dissertation meets
the requirements of the Dissertation Committee

Stephenie C. Lemon, Ph.D., Chair of Committee

The signature of the Dean of the Graduate School of Biomedical Sciences signifies that the student has met
all graduation requirements of the school

Anthony Carruthers, Ph.D.,
Dean of the Graduate School of Biomedical Sciences

Clinical and Population Health Research Program

April 6, 2015

ACKNOWLEDGEMENTS

Completion of this work was made possible with the guidance, support, and involvement of many individuals.

I am indebted to Dr. Kate Lapane, my dissertation advisor, for her unparalleled mentorship and for encouraging me to pursue an area of research consistent with my longstanding interests. I am very grateful for the enthusiastic support and patience of my thesis research advisory committee and dissertation examination committee members, Drs. Jerry Gurwitz, Allison Rosen, Stephenie Lemon, Robert Goldberg, and Beatriz Korc-Grodzicki. I would also like to express my sincere thanks to Dr. Becky Briesacher for her mentorship, friendship, and for teaching me to always think critically. The dedication of these faculty members ensured that I produced a body of work of which I am incredibly proud.

I would like to acknowledge my classmates in the Clinical and Population Health Research Program for their years of friendship, and my colleagues in the Department of Quantitative Health Sciences for providing me with an ideal research environment.

Special thanks go to my parents, Carlos and Jesusa Benedicto and Mariano and Consolacion Pimentel, who supported me during my tough days and who also celebrate my success as their own.

Finally, my deepest gratitude goes to my husband Marc, my collaborator in life *and* research, and my daughter Marie, my constant companion and source of great joy during the final nine months of my doctoral studies.

ABSTRACT

Nursing homes are an essential yet understudied provider of cancer-related care for those with complex health needs. Nine percent of nursing home residents have a cancer diagnosis at admission, and it is estimated that one-third of them experience pain on a daily basis. Although pain management is an essential component of disease treatment, few studies have evaluated analgesic medication use among adults with cancer in this setting. Use of opioids, which are the mainstay of pain management in older adults because of their effectiveness in controlling moderate to severe pain, may be significantly related to coverage by the Medicare Part D prescription drug benefit. However, little is known about Medicare Part D's effects on opioid use in this patient population. A limited body of evidence also suggests that despite known risks of overdose and respiratory depression in opioid-naïve patients treated with long-acting opioids, use of these agents may be common in nursing homes.

This dissertation examined access to appropriate and effective pain-related health care services among US nursing home residents, with a special focus on those with cancer. Objectives of this dissertation were to: 1) estimate the prevalence, and identify resident-level correlates, of pain and receipt of analgesic medications; 2) use a quasi-experimental research design to examine the relationship between implementation of Medicare Part D and changes in the use of fentanyl patches and other opioids; and 3) to estimate the prevalence, and identify resident-level correlates, of naïve initiation of long-acting opioids. Data on residents' health status from the Resident Assessment Instrument/Minimum Data Set (versions 2.0 and 3.0) were linked with prescription drug

transaction data from a nationwide long-term care pharmacy (January 2005–June 2007) and the Centers for Medicare and Medicaid Services (January–December 2011).

From 2006 to 2007, more than 65% of residents of nursing homes throughout the US with cancer experienced pain (28.3% on a daily basis), among whom 13.5% reported severe pain. More than 17% of these residents who experienced daily pain received no analgesics (95% confidence interval [CI]: 16.0–19.1%), and treatment was negatively associated among those with advanced age, cognitive impairment, feeding tubes, and restraints. These findings coincided with changing patterns in opioid use among residents with cancer, including relatively abrupt 10% and 21% decreases in use of fentanyl patches and other strong opioids, respectively, after the 2006 implementation of Medicare Part D. In the years since Medicare Part D was introduced, some treatment practices in nursing homes have not been concordant with clinical guidelines for pain management among older adults. Among a contemporary population of long-stay nursing home residents with and without cancer, 10.0% (95% CI: 9.4–10.6%) of those who began receiving a long-acting opioid after nursing home admission had not previously received opioid therapy. Odds of naïve initiation of these potent opioids were increased among residents with terminal prognosis, functional impairment, feeding tubes, and cancer.

This dissertation provides new evidence on pharmaceutical management of pain and on Medicare Part D's impact on opioid use in nursing home residents. Results from this dissertation shed light on nursing home residents' access to pain-related health care services and provide initial directions for targeted efforts to improve the quality of pain treatment in nursing homes.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

LIST OF ABBREVIATIONS

ADL	activity of daily living
CI	confidence interval
CMS	Centers for Medicare and Medicaid Services
FDA	Food and Drug Administration
IRR	incidence rate ratio
MDS	Minimum Data Set
NDC	National Drug Code
OR	odds ratio
REMS	Risk Evaluation and Mitigation Strategy
WHO	World Health Organization

PREFACE

Some of the work presented in this dissertation was published; will be published; is currently under review; or has been submitted for peer-reviewed publication.

Chapter II:

Pimentel CB, Briesacher BA, Gurwitz JH, Rosen AB, Pimentel MT, Lapane KL. Pain management in nursing home residents with cancer. Journal of the American Geriatrics Society 2015 Apr;63(4):633–41.

Chapter III:

Pimentel CB, Lapane KL, Gurwitz JH, Rosen AB, Briesacher BA. Should opioid pain medications receive special Medicare Part D coverage protection for nursing home residents with cancer? (Prepared for submission)

Chapter IV:

Pimentel CB, Gurwitz JH, Tjia J, Hume AL, Lapane KL. Naïve initiation of long-acting opioids in nursing home residents. (Prepared for submission)

CHAPTER I:

INTRODUCTION

1.1 Specific Aims

Approximately 1.6 million Americans are expected to be diagnosed with cancer in 2015,[1] with more than half of these new diagnoses of cancer occurring among adults aged ≥65 years.[2] As the provision of continuing care for older adults has shifted away from the hospital setting, nursing homes have become an essential yet understudied provider of cancer care for those with complex health needs.[3] Of an estimated 1.4 million nursing home residents,[4] nearly 9% have an active cancer diagnosis at admission.[5] Pain, one of the most common side effects of cancer, is experienced on a daily basis by upwards of one-third of nursing home residents with cancer.[6] Although management of cancer-related pain is an essential component of disease treatment, more than one-quarter of nursing home residents with severe pain may not receive any analgesics.[6] A limited number of studies have estimated the prevalence of cancer-related pain in nursing homes,[3,6] but few have characterized its pharmacologic treatment.

Opioids are the mainstay of cancer-related pain management among older adults because of their effectiveness in controlling moderate to severe pain.[7,8] Clinical guidelines recommend a sequential approach from the use of oral non-opioids for mild pain to the use of opioids for persons with more intense pain.[9,10] Longitudinal studies that describe patterns of opioid use among nursing home residents with cancer are lacking.

Opioid use in nursing home residents may be significantly related to coverage by the Medicare Part D prescription drug benefit that was implemented on January 1, 2006, and replaced Medicaid as the primary source of prescription drug coverage in nursing homes. Although Medicare Part D was created to improve Medicare beneficiaries' access

to essential medications, it may have had unintended consequences for nursing home residents who suffer from cancer-related pain. Prescription drug plans that privately administer Medicare Part D are required to cover "all or substantially all" medications in six classes commonly used by older adults;[11] however, broad coverage of opioids is not required even though they are the most commonly used analgesics in nursing homes.[12] Long-term care pharmacy claims for opioids are among the most frequently rejected by Medicare Part D plans, with rejections for administrative reasons increasing from 16% in 2007 to 28% in 2010.[13] Limited evidence exists on Medicare Part D's effects on opioid use among nursing home residents with cancer.

This dissertation examined access to appropriate and effective pain-related health care services among adults with cancer and a more general population of older adults who resided in US nursing homes. The specific aims of this dissertation were as follows:

Aim 1. We estimated the prevalence and resident-level correlates of pain and analgesic medication receipt among nursing home residents with cancer.

Aim 2. We used a quasi-experimental research design to examine the extent to which the implementation of Medicare Part D was associated with changes in fentanyl patch and other opioid use among nursing home residents with cancer.

Hypothesis: There would be a reduction in fentanyl patch use after the January 1, 2006, implementation of Medicare Part D.

Aim 3. We evaluated the prevalence and resident-level correlates of naïve opioid initiation in nursing home residents who receive a long-acting opioid within 30 days of nursing home admission.

1.2 Background and Significance

1.2.1 Cancer and Cancer-Related Pain in Older Adults

Adults aged 65 years and older represented 14.1% of the US population in 2013,[14] and this estimate is expected to increase to 19.3% by 2030.[15] Approximately 1.6 million Americans are expected to be diagnosed with cancer in 2015, with 78% of new diagnoses occurring among adults aged ≥55 years.[1] Cancer is the second leading cause of death in adults aged ≥65 years, accounting for approximately 403,000 deaths in older adults in 2012.[16]

Pain is the most common symptom of cancer in older adults.[17,18] More than half of individuals with cancer experience pain, regardless of cancer type, and more than one-third rate their pain as moderate or severe.[19] Pain is prevalent across the continuum of cancer care: 59% of individuals undergoing active treatment, 33% of those whose cancer is in remission, and 64% of those with metastatic, advanced or terminal disease experience pain.[19] Inadequately-treated pain has numerous psychological and physiological consequences, including depression, anxiety, sleep disturbance, decreased socialization, and impaired mobility.[20–22]

1.2.2 Opioid Use for Cancer-Related Pain Management

Opioid analgesics are highly effective in controlling moderate to severe pain and are the mainstay of cancer-related pain management among older adults.[7,8] Opioids are central to established clinical practice guidelines for adult cancer pain management, including those published by the World Health Organization (WHO)[9] and the National Comprehensive Cancer Network, an alliance of 21 National Cancer Institute-designated cancer centers.[10] These guidelines recommend a sequential analgesic therapy intensification approach from the use of non-opioids for mild pain to the use of opioids for more intense pain.[9,10] Duration of analgesic effect should also be carefully considered to prevent inadvertent overdose, with use of short-acting opioids advised for patients who are not chronically receiving opioid therapy and, therefore, have not developed significant tolerance to side effects (e.g., drowsiness, respiratory depression).[10,23] Use of the clinical practice guidelines is 80-90% effective at managing cancer-related pain overall.[9,24,25]

1.2.3 Pain Management in Nursing Homes

As the provision of continuing care for older adults has shifted away from acute care settings, nursing homes have become essential providers of cancer care.[3] Of an estimated 1.4 million nursing home residents,[4] nearly 9% have an active cancer diagnosis at admission.[5] Nursing homes are expected to carry more of the burden of cancer care delivery, given a 40% lifetime risk of nursing home placement after age 65 years,[26–28] rising prevalence of cancer among a growing older adult population, and improvements in life expectancy after a cancer diagnosis.[29] Approximately 31.3% of Medicare

beneficiaries with cancer receive nursing home care in the last 90 days before death, and 17.1% die in the nursing home.[30] An estimated 29.4% of nursing home residents with cancer experience pain on a daily basis.[6]

Despite this finding, a limited number of studies have critically evaluated patterns and correlates of analgesic use in nursing home residents. Rigler and colleagues documented that use of long-acting opioids is more common among nursing home residents than older adults living in the community.[31] Data describing analgesic use in nursing home residents suggest that opioids are the most commonly used class (67.6% compared to 24.8% for non-steroidal anti-inflammatory drugs).[12] Yet, how opioids are used may not be guideline concordant. Dosa and colleagues estimated that 39.3% of nursing home residents (10.8% of whom had cancer) who received a long-acting opioid were previously opioid-naïve, despite Food and Drug Administration (FDA) public health advisory warnings of morbidity and death associated with initiation of these potent agents in new opioid users.[32] Naïve initiation of long-acting opioids was more frequent among nursing home residents with advanced age and increased cognitive impairment. Data specifically describing analgesic use among patients with cancer in nursing homes are scant. The most comprehensive study to date (published in 1998) found that among nearly 14,000 nursing home residents with cancer, 26% of those with daily cancer pain did not receive any analgesics.[6] Advanced age, minority race, increasing numbers of other medication[6] and low cognitive performance[6,33,34] were associated with failure to receive analgesics, even at the end of life.[33,34]

1.2.4 Impact of Medicare Part D on Opioid Use for Cancer-Related Pain Management

Medicare Part D, the Medicare prescription drug benefit, may have influenced opioid use in nursing homes. Implemented on January 1, 2006, Medicare Part D replaced Medicaid as the primary source of prescription drug coverage in nursing homes. An estimated 63% of nursing home residents who were dually eligible for Medicaid and Medicare were automatically enrolled in Medicare Part D,[35] and another one-third of Medicare-only residents voluntarily enrolled. Medicare Part D prescription drug plans are not required to cover opioids, owing to concerns about inappropriate use among Medicare beneficiaries.[36] Long-term care pharmacy claims for opioids are among the most frequently rejected by Medicare Part D plans, with rejections for administrative reasons increasing from 16% in 2007 to 28% in 2010.[13] Although Medicare Part D was created to improve access to essential medication, it may have had unintended consequences for those who suffer from cancer-related pain.

Evidence of Medicare Part D's impact on opioid use in nursing homes is limited but suggestive of barriers to opioids for cancer-related pain management. Long-term care pharmacy claims for generic fentanyl and hydrocodone-acetaminophen combinations were among the most frequently rejected by Medicare Part D prescription drug plans in 2006.[37] Generic opioids remained among the most commonly rejected prescription drugs in 2010, with rejections of nearly one-third of claims for oxycodone, oxycodone-acetaminophen combinations, extended-release morphine sulfate, and transdermal fentanyl systems.[13] There is evidence of relationships between Medicare Part D and

decreased use of medications that carry safety concerns when used to treat older adults.[38] There have not been any studies of Medicare Part D's impact on both opioid use and cancer patients residing in nursing homes.

1.3 Research Design and Methods

1.3.1 Data Sources

Aims 1 and 2

A nationwide long-term care pharmacy provided data for Aims 1 and 2 under a data use agreement. Data included nursing home resident health assessments from the Resident Assessment Instrument/Minimum Data Set (MDS) version 2.0 linked with all-payer administrative records of all dispensed prescription and over-the-counter medication.

MDS 2.0 is a systematic and comprehensive assessment of care planning and resident health that consists of more than 400 items, including sociodemographic information, clinical characteristics (e.g., cognitive patterns, communication, mood and behavior, signs, symptoms), active clinical diagnoses, and treatments provided.[39,40] It includes multi-item summary scales for measures of functional status (Activities of Daily Living [ADL] Hierarchy Scale),[41] depressed mood (Depression Rating Scale),[42] and cognitive status (Cognitive Performance Scale).[43] Long-term care facilities that participate in the Medicare and Medicaid programs (approximately 96% of all US facilities) are required to perform full MDS assessments on residents at admission and annually; a subset of the MDS items are assessed quarterly or when a resident

experiences a significant change in health status.[39] A registered nurse performs the assessment of a resident's status over the previous seven days based on medical record review, direct observation of and communication with the resident, family interviews, and discussions with the resident's medical and direct care teams.

The long-term care pharmacy linked the MDS assessments to drug dispensing records using unique study identifiers. Drug data came from more than 2.5 million residents of approximately 16,000 nursing homes across 48 states. The drug dispensing records were of all medications dispensed to nursing home residents from January 1, 2005, to June 30, 2007. Data elements included brand and generic names, product identification code (National Drug Code [NDC]), prescription date, days' supply, quantity dispensed, and payment source (i.e., cash, Medicaid, private insurance, Medicare Parts A/B, Medicare Part D, and facility/hospice). Resident-level information included age, sex, and state of nursing home residence.

Aim 3

The Centers for Medicare and Medicaid Services (CMS) provided data for Aim 3 under Data Use Agreement 26885. Data included: 1) nursing home resident health assessments from the Resident Assessment Instrument/MDS version 3.0, 2) Master Beneficiary Summary Files that determine Medicare enrollment, 3) MedPar files containing hospital claims data, and 4) Medicare Part D prescription drug transaction data.

MDS 3.0 is a revision of MDS 2.0 and was implemented in all Medicare- and Medicaid-certified nursing homes in October 2010. It is a systematic and comprehensive assessment of care planning and resident health that consists of sociodemographic information; clinical items (e.g., falls and balance, bladder and bowel, communication, behavior, signs, symptoms); active diagnoses; and treatments, procedures, and programs.[44,45] MDS 3.0 multi-item summary scales exist for measurement of functional status (Resource Utilization Groups-III ADL)[46] and cognitive status (Cognitive Function Scale).[47] As in MDS 2.0, nursing home providers are required to perform full MDS assessments on residents at admission and annually, and a subset of the MDS items are assessed quarterly or when a resident experiences a significant change in health status.[44] The most significant conceptual departure from MDS 2.0 is the inclusion of direct resident interviews to assess key domains of health. Although resident interviews are the preferred method for completing the assessment, nursing home staff may answer alternative observation items on behalf of residents who cannot make themselves understood at least some of the time or who cannot complete an interview. Family members or significant others may answer items regarding resident preferences.

CMS provided a unique study identifier to link the MDS assessments to Medicare Part D prescription drug transactions (i.e., event and characteristics files). The transactions were for all Medicare Part D-reimbursed prescription medications dispensed to nursing home residents from January 1, 2011, to December 31, 2011. Data elements in the event file included product identification code (NDC), service date, days' supply, and quantity dispensed. Data elements from the characteristics file included brand and generic

names, drug strength, and drug formulation, and the Multum® drug database was used to map drug names to therapeutic categories. Beneficiary-level information included dates of Medicare Part D enrollment and death.

1.3.2 Study Designs and Populations

Aim 1

We conducted a cross-sectional study for this study aim. **Figure 1-1** shows the sample selection strategy. The sampling frame consisted of nursing home residents with MDS assessments performed between February 1, 2006, and June 30, 2007 (n = 166,139). We included in our sample nursing home residents with a cancer diagnosis indicated on MDS assessment (n = 23,485). A cancer diagnosis was indicated by a check box under MDS "Section I. Disease Diagnoses" and reported only if the diagnosis was related to "current ADL status, cognitive status, mood and behavior status, medical treatments, nursing monitoring, or risk of death" and not inactive.[39]

We excluded nursing home residents admitted to the nursing home before February 1, 2006 (n = 13,452). Newly-admitted residents were those who had an MDS assessment performed at admission (i.e., by day 14). We also excluded nursing home residents whose prescriptions could not be identified using NDCs (n = 1,633) and who were not eligible for Medicare (n = 25). Medicare-eligibility was indicated by age ≥65 years or, for younger nursing home residents, receipt of ≥1 Medicare-paid prescription drug. Finally, we excluded nursing home residents who were comatose (n = 7) and who were missing information on key sociodemographic and clinical characteristics (n = 274).

The final sample size was 8,094 nursing home residents who were admitted to 1,382 nursing homes throughout the US.

Aim 2

We conducted a segmented Poisson regression of interrupted time-series. **Figure 1-2** shows the sample selection strategy. The sampling frame consisted of nursing home residents with MDS assessments performed between January 1, 2005, and June 30, 2007 (n = 234,308). We included in our sample nursing home residents with a cancer diagnosis indicated on MDS assessment (n = 23,485). A cancer diagnosis was indicated by a check box under MDS "Section I. Disease Diagnoses" and reported only if the diagnosis was related to "current ADL status, cognitive status, mood and behavior status, medical treatments, nursing monitoring, or risk of death" and not inactive.[39]

We excluded residents who were not eligible for Medicare at any point during the study (n = 1,320). Medicare-eligibility was indicated by age ≥65 years or, for younger nursing home residents, receipt of ≥1 Medicare-paid prescription drug. We also excluded residents who resided in facilities that lacked pharmacy dispensing records in both pre- and post-Medicare Part D periods (n = 2,383) and who were missing information on key sociodemographic and clinical characteristics (n = 1,183).

The final sample size was 18,599 nursing home residents who were admitted to 1,112 nursing homes.

Aim 3

We conducted a cross-sectional study for this study aim. **Figure 1-3** shows the sample selection strategy. The sampling frame consisted of Medicare-enrolled nursing home residents with an admission assessment performed between January 1, 2011, and December 31, 2011 (n = 3,273,636). We required that residents have a nursing home stay ≥90 days (n = 1,103,195), as Medicare Part D prescription drug transactions may not include medications associated with skilled nursing facility care covered by Medicare Part A. We excluded residents who were comatose (n = 3,479); who were admitted to the nursing home between January 1, 2011, and March 31, 2011 (n = 130,598); who did not initiate a long-acting opioid after nursing home admission (n = 949,965); who did not have three months of continuous enrollment in Medicare Part D prior to initiation of a long-acting opioid in the nursing home (n = 1,176); who had a hospital admission in the seven days prior to initiation of a long-acting opioid in the nursing home (n = 874); or who were missing information on key sociodemographic or clinical characteristics (n = 1,041). We identified 16,062 nursing home residents who met these eligibility criteria. Although we estimated the proportion of residents naively initiating a long-acting opioid using several subsamples derived from this population, the primary analysis was conducted in 9,543 residents who were admitted to 3,018 facilities and who initiated a long-acting opioid in the first 30 days of admission.

1.3.3 Measures

Outcome Variables (Aim 1)

Pain. MDS 2.0 defines pain as any type of physical pain or discomfort in any part of the body occurring daily over the seven days preceding the assessment. It includes one item for frequency of pain, rated as no pain, less than daily, and daily, and one item for pain intensity, rated as mild, moderate, or horrible/excruciating. The MDS instructions for these measures recommend reliance on resident self-report whenever possible, although family and staff observations may also be used. The reliability of these items exceeds intraclass correlation of 0.70[48] and a summary scale based on these items has been validated with the vertical Visual Analog Scale.

Analgesic use. The long-term care pharmacy that provided data for Aim 1 also furnished a drug dictionary that we used to translate NDCs from the drug dispensing records into therapeutic classes and sub-classes. Analgesics are listed in **Table 1-1** and were classified as non-opioids, mild opioids, and strong opioids according to the WHO "ladder" for cancer pain relief;[9,24,25] by formulation (e.g., oral, intravenous/intramuscular, transdermal, suppository); and by duration of effect (i.e., short-acting, long-acting).

Outcome Variables (Aim 2)

Opioid use: We created four categories of analgesics: 1) all opioids typically used to treat moderate to severe pain (WHO level 3 drugs); 2) fentanyl patches; 3) potential fentanyl patch substitutes (i.e., other WHO level 3 drugs); and 4) opioids used for mild to

moderate pain (WHO level 2 drugs). Fentanyl patches included branded and generic medications. Other WHO level 3 drugs included oral and injectable formulations of fentanyl, morphine, hydromorphone, oxycodone, oxymorphone, methadone, buprenorphine, and meperidine.[49] WHO level 2 drugs included codeine, hydrocodone, propoxyphene, pentazocine, butorphanol, standardized opium, tramadol, and any combination of these drugs with non-steroidal anti-inflammatory drugs and acetaminophen.[49] For each of the four categories of analgesics, we created two outcome measures: 1) monthly proportion of nursing home residents receiving ≥1 prescription of interest and 2) monthly proportion of resident-therapy days covered. Outcomes were examined from January 2005 through December 2005 (pre-Medicare Part D implementation) and from February 2006 through June 2007 (post-Medicare Part D implementation).

Outcome Variables (Aim 3)

Naïve initiation of long-acting opioid. We categorized opioid analgesics by duration of effect (i.e., long-acting, short-acting) according to recent clinical practice guidelines that consider pain management by level of opioid-tolerance.[10,50,51] Long-acting opioids included controlled- or extended-release formulations of hydromorphone, morphine sulfate, oxycodone, oxymorphone, and tramadol, as well as any dose of fentanyl patch and buprenorphine patch. Brand and generic names are listed in **Table 1-1**. Short-acting opioids included immediate-release formulations of buprenorphine, butorphanol, codeine, fentanyl, hydrocodone, hydromorphone, meperidine, morphine sulfate, nalbuphine,

opium, oxymorphone, oxycodone, pentazocine, tapentadol, and tramadol. Opioids combined with acetaminophen or non-steroidal anti-inflammatory drugs, which limit the maximum daily dose because of risks of liver and gastrointestinal toxicity, were also considered short-acting.[52]

We evaluated the first 30 days of a nursing home stay based on the expectation that initial provision of analgesic medications would occur shortly after admission. Nursing home residents were considered opioid-naïve if they had not used a short- or a long-acting opioid in the 60 days preceding initial receipt of a long-acting opioid after nursing home admission.

Correlates

Correlates were selected based on previous literature and drawn from MDS assessments and drug dispensing records. They included the key sociodemographic and clinical characteristics listed in **Table 1-1.**

1.3.4 Statistical Analysis

Descriptive Statistics (Aims 1, 2, and 3)

We presented means, standard deviations, and ranges for continuous variables and proportions for categorical variables. We compared means using t-tests and proportions using Chi-square tests.

Multivariable Analysis (Aims 1 and 3)

We developed a multinomial logistic model to estimate the effects of resident-level characteristics on the likelihood of having pain (Aim 1), and binary logistic models to estimate the likelihood of receiving an analgesic (Aim 1) and naïve initiation of a long-acting opioid after nursing home admission (Aim 3). Before constructing the models, we calculated correlations among variables. If variable pairs were highly collinear (>0.90), only one of the variables was included in the final models. The logistic models were fit using robust estimation of standard errors to adjust for clustering effects of residents within nursing homes.[53]

In Aim 1, models were manually constructed in a step-wise fashion, with variables with $P \leq 0.25$ in univariate tests retained in the final models. Based on previous work,[6] we did not anticipate interactions among covariates; however, we evaluated and ruled out interactions. We used the Hosmer-Lemeshow test to evaluate goodness-of-fit, and McFadden pseudo-R^2 and the c-statistic to assess model discrimination, with a c-statistic ≥0.80 indicating a strong model.[54]

In Aim 3, models were adjusted for all correlates of interest. Adjusted odds ratios (ORs) and 95% confidence intervals (CIs) were derived from the final models.

Time Series Analysis (Aim 2)

Interrupted time series, a strong quasi-experimental research design well-suited for evaluations of time-delimited interventions,[55] was used to assess the longitudinal effects of Medicare Part D on fentanyl patch and other opioid use. First, time series data

were visually analyzed for noticeable changes in level and trend of opioid use between the time segments before and after Medicare Part D implementation. Second, segmented regression analysis was used to assess whether changes in level and trend were the result of chance or factors other than Medicare Part D. A least squares regression line was fit to each segment of the predictor, *time*; however, after evaluation of the linearity of the relationship between prescribing rates and *time* within each of the two time segments, we decided to fit a Poisson model that is more appropriate for counts of rare events.[56] We developed a segmented regression model using a generalized linear model approach to estimate the immediate change in the prescribing rate level and the gradual change in trend after the implementation of Medicare Part D, adjusting for baseline level and trend. The basic model is:

$$Y_t = \beta_0 + \beta_1 time_t + \beta_2 Part\ D_t + \beta_3 time\ after\ Part\ D_t + \varepsilon_t$$

where Y_t is the prevalence of opioid use per month t; $time$ is the underlying time trend (a continuous variable indicating time in months at time t from the start of the observation period); $Part\ D$ is an indicator for time t occurring before ($Part\ D = 0$) or after Medicare Part D ($Part\ D = 1$), which was implemented at month 13 in the series; and $time\ after\ Part\ D$ is a continuous variable indicating the number of months after Part D at time t, coded 0 before Medicare Part D and ($time - 12$) after Medicare Part D. β_0 estimates the baseline level of opioid use prevalence per month; β_1 estimates the change in opioid use prevalence that occurs each month before Medicare Part D (i.e., the baseline trend); β_2 estimates the level change in opioid use prevalence immediately after

Medicare Part D implementation; and β_3 estimates the change in the trend in opioid use prevalence after Medicare Part D implementation, compared with the monthly trend before Medicare Part D. The sum of β_1 and β_3 represents the post-Medicare Part D slope. The error term, ε_t , at time t represents the random variability not explained by the model. Specifically, ε_t consists of a normally distributed random error and an error term at time t that may be correlated to errors at preceding or subsequent time points. We adjusted this basic model for rates for January 2006 (a dummy variable for this transition month), and evaluated and ruled out seasonal effect (dummy variables for quarters in each calendar year).

Error terms of consecutive observations may be correlated, and failure to correct for this may lead to an underestimation of standard errors and an overestimation of the effects of Medicare Part D.[55] Autocorrelation of the error terms in the segmented regression model were evaluated by visual inspection of residual plots and the Durbin-Watson statistic.[57,58] Random patterns among residuals plotted against time indicated no autocorrelations; positive and negative autocorrelations would have been indicated if consecutive residuals lined on the same side or different sides of the regression line, respectively.[57] A Durbin-Watson test statistic of 2.00 indicated no serious autocorrelation.[58] However, we fit our segmented regression models using Newey-West standard errors to account for possible serial correlation of consecutive observations.[59]

Adjusted incidence rate ratios (IRR) and 95% CIs were derived from the final models. $P \leq 0.05$ (two-tailed) was considered statistically significant.

1.4 Innovations and Impact

The innovation of this dissertation lies in its topic area and the unique data sources and methodological approaches used. First, this dissertation sought to explore a population not well studied – nursing home residents with cancer. Research to date has been limited to sub-groups of cancer patients in nursing homes, specifically those who were admitted to the nursing home from a hospital[6] or decedents with comorbid dementia.[33,34] This dissertation provides new evidence relevant to a broad population of cancer patients in nursing homes. It contributes much-needed empirical evidence on the pharmaceutical management of cancer-related pain in nursing homes, a critical public health issue of increasing importance. The most comprehensive evaluation of cancer-related pain management in this setting[5] was based on data from nearly 20 years ago and, in the years since, the landscape of pain management in nursing homes may have changed. By examining access to appropriate and effective pain management among cancer patients in US nursing homes, this dissertation promotes research on quality of health care services in a particularly vulnerable segment of the older adult population. Second, we used in Aims 1 and 2 a unique, nationally-representative administrative database spanning a variety of payment sources, including Medicare, Medicaid, private insurance, cash, and facility/hospice. Previous studies have examined only single-payer data sources such as Medicaid and Medicare. This innovative dataset permits the evaluation of all patients with cancer-related pain in nursing homes, regardless of payer status. Third, we used the richness of this longitudinal data source to understand naïve initiation of long-acting opioids. Such detailed information may provide new

opportunities for improving pain management in this setting. Additionally, the increasing use of nursing homes as a setting for cancer care, and the shift of most nursing home residents from Medicaid to Medicare Part D as the payer for medication in this setting, underscores the need for an evaluation of the impact of Medicare Part D on this often understudied, yet vulnerable, population. Fourth, the use of segmented regression of interrupted time series to empirically evaluate the impact of a national policy change on opioid use is novel. This analytic method is considered to be the strongest quasi-experimental design to evaluate the effects of time-delimited interventions.[55]

The significance of this work rests with the potential to stimulate change in health policy and practice through the provision of needed information about the potential unintended effect of Medicare Part D on older men and women with cancer experiencing pain. As the first empirical evaluation of Medicare Part D's impact on opioid use among patients with cancer in nursing homes, this dissertation provides stimulus for enhanced Medicare Part D coverage of essential pain medication for Medicare beneficiaries residing in nursing homes. In particular, opioids may be considered a protected drug class that Medicare Part D prescription drug plan formularies are expected to carry. In addition, this dissertation offers new information that could promote new directions for interventions to enhance the quality of cancer-related pain management in nursing homes nationwide. Study results may have direct implications for long-term care clinical practice and policy by providing measures of cancer-related pain and analgesic use to inform targets for nursing home quality improvement efforts. Shortly after publication of the first evaluation of cancer-related pain management quality among nursing home

residents,[5] CMS quality indicators focusing on pain management in nursing homes were implemented and publicly reported.[60,61] Similarly, the Robert Wood Johnson Foundation launched a national program, "Targeted End-of-Life Projects Initiative," to improve care at the end of life. A 1999 recommendation from this initiative was that states should assess whether their laws and regulations inadvertently act as barriers to pain management by discouraging the use of opioids.[62]

Figure 1-1: Sample Selection Strategy for Aim 1

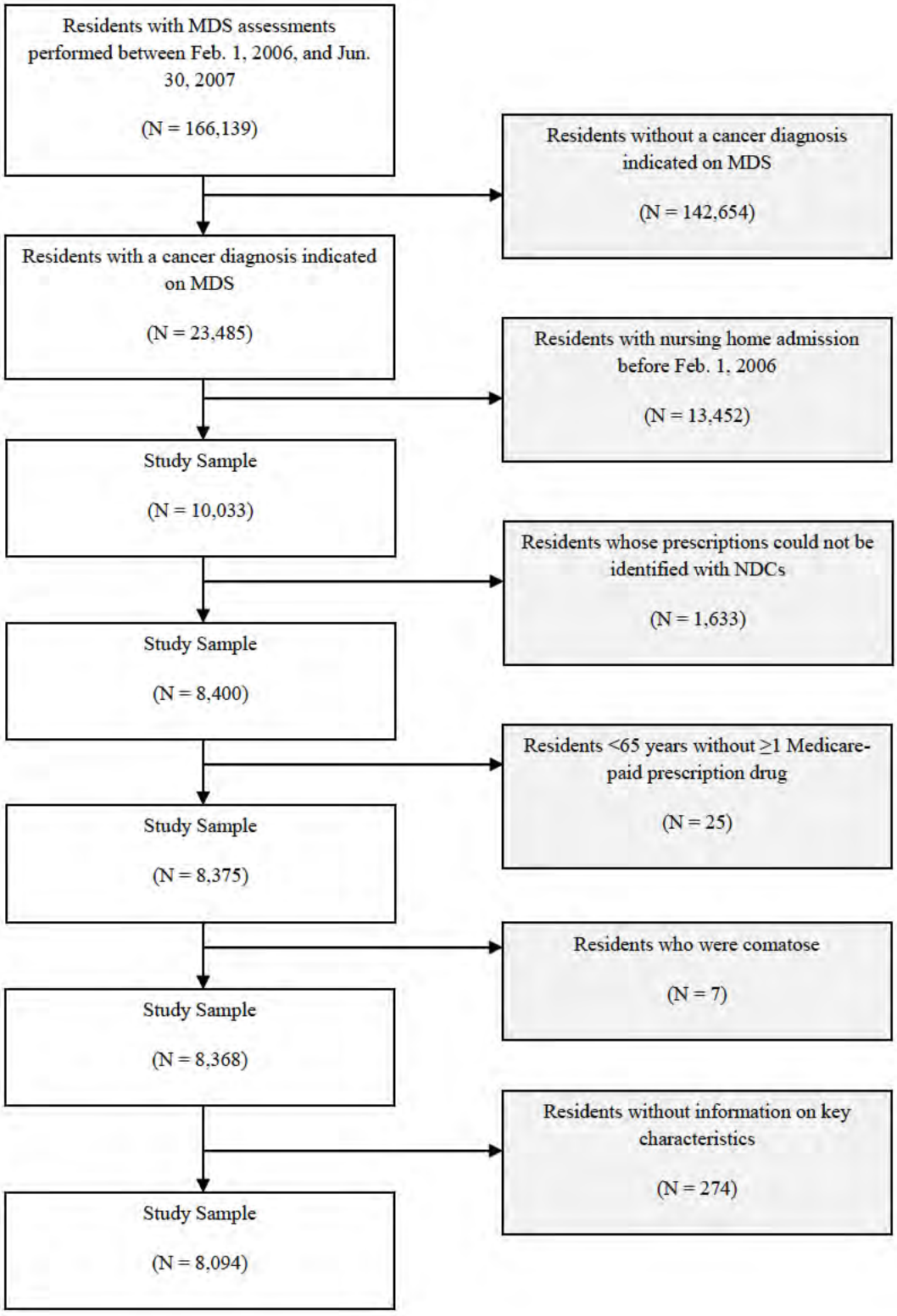


Figure 1-2: Sample Selection Strategy for Aim 2

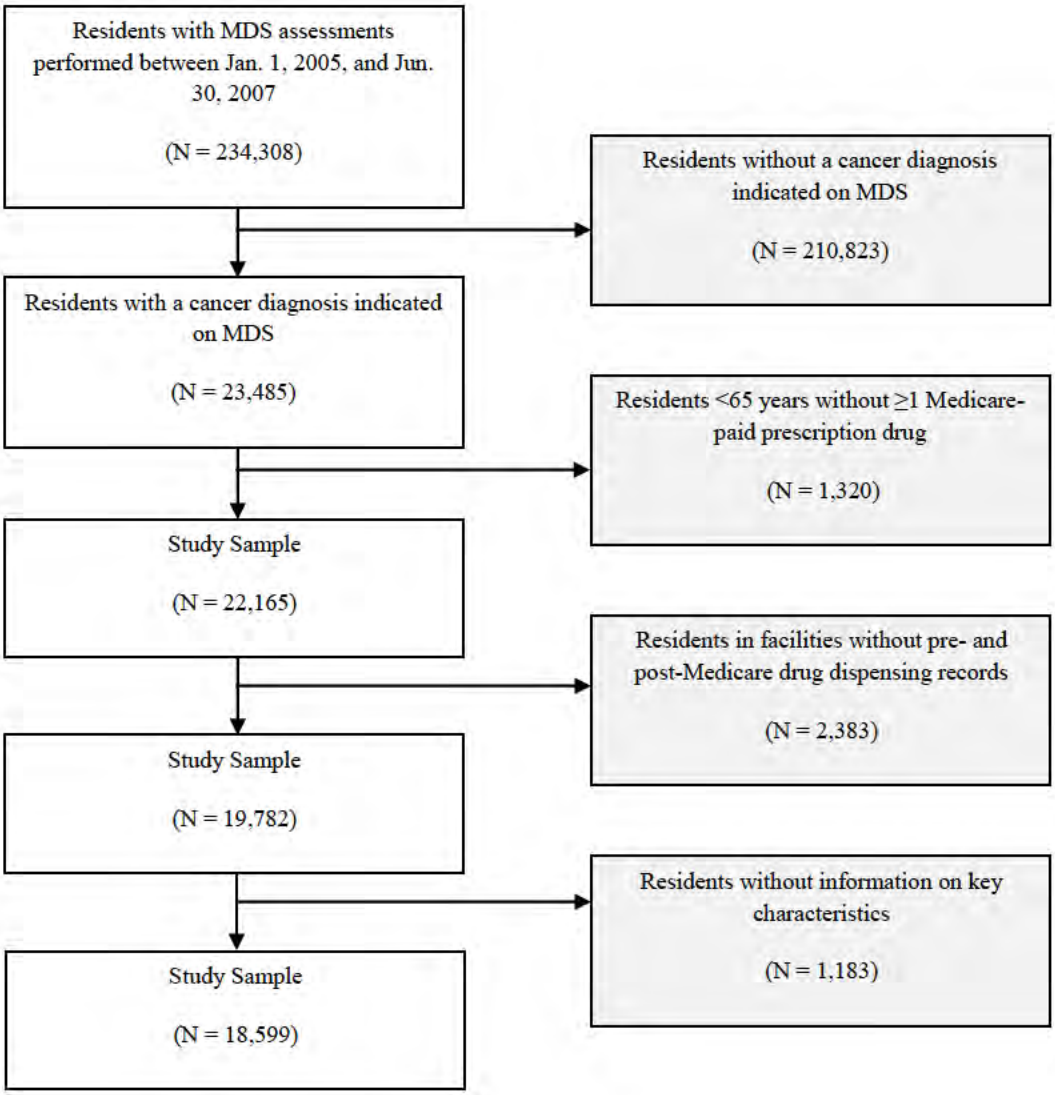


Figure 1-3: Sample Selection Strategy for Aim 3

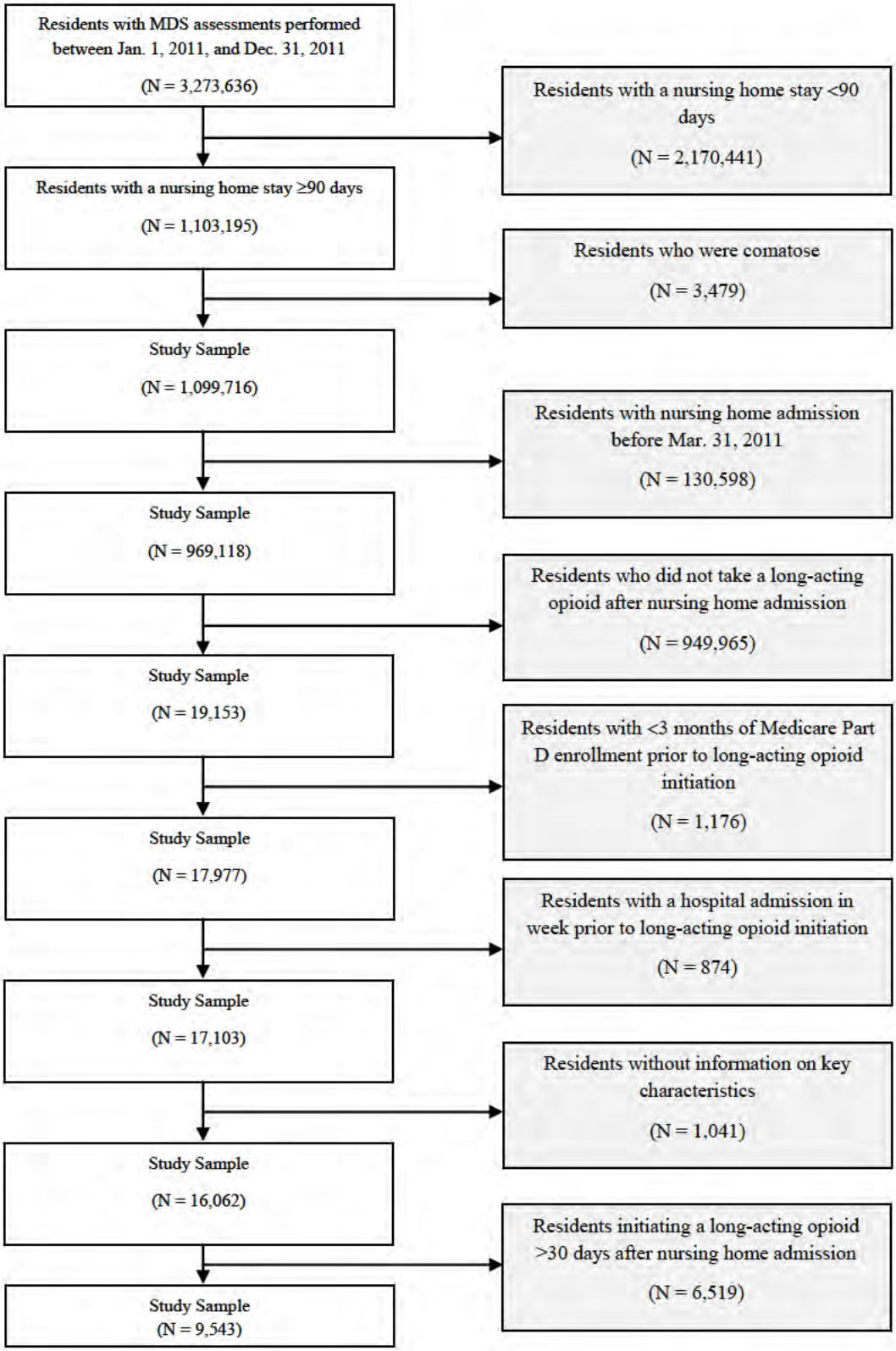


Table 1-1: Variable Definitions, Coding, and Source

Variable	Definition	Coding	Source
Sociodemographics			
Age		Categorical: <65, 65–74, 75–84, ≥85	Drug dispensing records, MDS 3.0
Sex		Dichotomous	MDS 2.0, 3.0
Race/ethnicity		Categorical: non-Hispanic white, non-Hispanic black, Hispanic, Asian, Native Hawaiian or other Pacific Islander, American Indian or Alaska Native, multiracial	MDS 2.0, 3.0
Marital status		Categorical: never married, married, widowed, separated or divorced	MDS 2.0
Region	US Census Region	Categorical: South, West, Midwest, Northeast	Drug dispensing records
Clinical Characteristics			
Source of admission		Categorical: acute care hospital, private home, other nursing home, other	MDS 2.0, MDS 3.0
Functional status	Score on Activities of Daily Living (ADL) Hierarchy Scale[41]	Categorical. Scores are between 0 and 6, where: 5–6 = severe impairment 3–4 = moderate impairment 0–2 = no/mild impairment	MDS 2.0
	Resource Utilization Groups-III ADL Score[46]	Categorical. Scores are between 4 and 18, where: 17–18 = severe impairment 14–16 = moderate impairment 0–14 = no/mild impairment	MDS 3.0
Cognitive status	Score on Cognitive Performance	Categorical. Scores are between	MDS 2.0

Variable	Definition	Coding	Source
	Scale[43]	0 and 6, where: 5–6 = severe impairment 2–4 = moderate impairment 0–1 = no/mild impairment	
	Score on Cognitive Function Scale[47]	Categorical: cognitively intact, mild impairment, moderate impairment, severe impairment	MDS 3.0
Depressed mood	Score on Depression Rating Scale[42]	Categorical. Scores are between 0 and 14, where: ≥3 = indication of major or minor depressive disorder	MDS 2.0
Terminal prognosis	Life expectancy of <6 months or receipt of hospice care	Dichotomous	MDS 2.0, MDS 3.0
Bedfast		Dichotomous	MDS 2.0
Parenteral feeding/feeding tube		Dichotomous	MDS 2.0, MDS 3.0
Indwelling catheter		Dichotomous	MDS 2.0
Restraints	Trunk and limb restraints and chairs to prevent rising	Dichotomous	MDS 2.0
Difficulty chewing		Dichotomous	MDS 3.0
Difficulty swallowing		Dichotomous	MDS 3.0
Rejected care		Dichotomous	MDS 3.0
Number of diagnoses		Continuous	MDS 2.0
Alzheimer disease		Dichotomous	MDS 3.0
Arthritis	e.g., degenerative joint disease, osteoarthritis, rheumatoid arthritis	Dichotomous	MDS 2.0, MDS 3.0
Asthma, chronic obstructive pulmonary disease, or chronic lung disease		Dichotomous	MDS 3.0
Cancer	With or without metastasis	Dichotomous	MDS 3.0
Heart failure	e.g., congestive heart failure, pulmonary edema	Dichotomous	MDS 3.0
Hip fracture	e.g., sub-capital fractures,	Dichotomous	MDS 2.0, MDS 3.0

Variable	Definition	Coding	Source
	fractures of the trochanter and femoral neck		
Osteoporosis		Dichotomous	MDS 2.0, MDS 3.0
Respiratory failure		Dichotomous	MDS 3.0
Stroke		Dichotomous	MDS 3.0
Number of medications		Continuous	Drug dispensing records
Outcome Variables			
Pain	Any pain in the 7 days preceding assessment	Dichotomous	MDS 2.0
	Any pain in the 5 days preceding assessment	Dichotomous	MDS 3.0
Frequency		Categorical: no pain, less than daily, daily	MDS 2.0
		Categorical: rarely, occasionally, frequently, almost constantly	MDS 3.0
Intensity		Categorical: mild, moderate pain, severe	MDS 2.0
	Numeric rating scale	Categorical. Scores are between 0 and 10, with: 0 = no pain 1–4 = mild 5–7 = moderate 8–9 = severe 10 = very severe/horrible[63]	MDS 3.0
	Verbal descriptor scale	Categorical: mild, moderate, severe, very severe/horrible	MDS 3.0
Receipt of analgesics		Dichotomous	Drug dispensing records
Receipt of WHO level 1 drug	Any record for: • Nonsteroidal anti-inflammatory drugs • acetaminophen	Dichotomous	Drug dispensing records

Variable	Definition	Coding	Source
Receipt of WHO level 2 drug	Any record for: • codeine • hydrocodone • propoxyphene • pentazocine • nalbuphine • butorphanol • standardized opium • tramadol • combinations of these drugs with WHO level 1 drug	Dichotomous	Drug dispensing records
Receipt of WHO level 3 drug	Any record for: • morphine • hydromorphone • oxycodone • oxymorphone • buprenorphine • methadone • meperidine • levorphanol • fentanyl	Dichotomous	Drug dispensing records
Receipt of adjuvants	Any record for: • corticosteroids • muscle relaxants • gabapentin • pregabalin • tricyclic antidepressants • selective norepinephrine reuptake inhibitors • alpha-2-adrenergic	Dichotomous	Drug dispensing records

Variable	Definition	Coding	Source
	agonists • transdermal lidocaine • mexiletine		
Receipt of long-acting opioid	Any record for: • Avinza® (morphine sulfate extended-release) • Butrans® (transdermal buprenorphine system) • Duragesic® (transdermal fentanyl system) • Exalgo® (hydromorphone hydrochloride extended-release) • Kadian® (morphine sulfate extended-release) • MS Contin® (morphine sulfate controlled-release) • Opana ER® (oxymorphone hydrochloride controlled-release) • Oxycontin® (oxycodone hydrochloride controlled-release) • Ultram ER® (tramadol hydrochloride) • methadone	Dichotomous	Drug dispensing records
Receipt of short-acting opioid	Any record for immediate-release formulations of: • buprenorphine • butorphanol • codeine	Dichotomous	Drug dispensing records

Variable	Definition	Coding	Source
	• fentanyl citrate • hydrocodone • hydromorphone • meperidine • morphine sulfate • nalbuphine • opium • oxymorphone • oxycodone • pentazocine • tapentadol • tramadol • combinations of these drugs with WHO level 1 drugs[52]		
Receipt of oral opioid		Dichotomous	Drug dispensing records
Receipt of transdermal opioid		Dichotomous	Drug dispensing records
Receipt of intravenous or Intramuscular opioid		Dichotomous	Drug dispensing records
Receipt of suppository opioid		Dichotomous	Drug dispensing records

CHAPTER II:

PAIN MANAGEMENT IN NURSING HOME RESIDENTS WITH CANCER

ABSTRACT

BACKGROUND: In the mid-1990s, 29.4% of nursing home residents with cancer suffered from daily pain, and among them 26% failed to receive any analgesics. Our objective was to assess improvements in pain management of nursing home residents with cancer since the implementation of pain management quality indicators.

METHODS: This cross-sectional study included 8,094 newly-admitted, Medicare-eligible nursing home residents with cancer admitted to 1,382 US nursing homes. Nationwide data from the MDS 2.0 linked to all-payer pharmacy dispensing records (February 2006-June 2007) were used to determine prevalence of pain, including frequency and intensity, and receipt of non-opioid and opioid analgesics. Multinomial logistic models evaluated resident-level correlates of pain and binomial logistic models identified correlates of untreated pain.

RESULTS: More than 65% of nursing home residents with cancer had any pain (28.3% daily, 37.3% less than daily), among whom 13.5% had severe and 61.3% had moderate pain. Women, residents admitted from acute care or who were bedfast, and those with compromised ADLs, depressed mood, indwelling catheter, or terminal prognosis were more likely to have pain. More than 17% of residents in daily pain (95% CI: 16.0–19.1%) received no analgesics, including 11.7% with daily severe pain (95% CI: 8.9–14.5%) and 16.9% with daily moderate pain (95% CI: 15.1–18.8%). Treatment was negatively associated with age ≥85 years (adjusted OR = 0.67, 95% CI: 0.55–0.81 versus aged 65–74), cognitive impairment (adjusted OR=0.71, 95% CI: 0.61–0.82), presence of feeding tube (adjusted OR = 0.77, 95% CI: 0.60–0.99), and restraints (adjusted OR = 0.50, 95% CI: 0.31–0.82).

CONCLUSION: Untreated pain is still common among nursing home residents with cancer and persists despite pain management quality indicators.

2.1 Introduction

Nursing homes are becoming an essential provider of cancer care for those whose complex health needs require continuous care. Among an estimated 1.4 million nursing home residents,[4] 9% have a cancer diagnosis at admission.[5] Approximately 31.3% of Medicare beneficiaries with cancer receive nursing home care in the three months before death, and 17.1% ultimately die in this setting.[30] Nursing homes are expected to carry more of the burden of cancer care delivery, given a 40% lifetime risk of nursing home placement after age 65 years,[26–28] rising prevalence of cancer among a growing older adult population, and improvements in life expectancy after a cancer diagnosis.[29]

Pain is the most common symptom in older adults with cancer,[17,18] and pain management is critical to providing optimal care to these patients. Widely regarded as the "fifth vital sign,"[64] pain deserves prompt evaluation and treatment. Clinical practice guidelines published by the WHO[49] serve as the foundation for guidelines by the American Society of Anesthesiologists,[50] European Society for Medical Oncologists,[51] and the National Comprehensive Cancer Network,[10] and have been shown to be 80–90% effective at managing cancer-related pain overall.[9,24,25] However, pain among patients with cancer is known to be undertreated in nursing homes. The most comprehensive evaluation thus far of pain management among nursing home residents with cancer, published in 1998, found that 29.4% of residents with cancer suffered from pain on a daily basis.[6] More than a quarter of those with daily pain failed to receive analgesics, and lack of treatment was significantly associated with advanced age, minority race, and cognitive impairment.[6] Similarly, studies of nursing home residents with comorbid

dementia and advanced cancer showed inverse relationships between cognitive ability and pain-related behaviors, and between cognitive ability and dose of opioid medication.[33,34]

National efforts have since been made to improve upon the quality of nursing home care, including the public reporting of the CMS pain management quality indicators beginning in 2002.[60] An update to our current understanding of pain management among nursing home residents with cancer is needed. Therefore, we examined the use of analgesics among more than 8,000 cancer patients residing in US nursing homes in 2006 and 2007. Specifically, we estimated the prevalence and resident-level correlates of pain and receipt of analgesics among newly-admitted older and disabled nursing home residents with cancer.

2.2 Methods

The institutional review board of the University of Massachusetts Medical School approved this study.

2.2.1 Data Sources

We used the most recent data available from a nationwide long-term care pharmacy, including nursing home resident health assessments from the MDS version 2.0 linked with an all-payer administrative data source of all dispensed prescription and over-the-counter medication.

The MDS is a federally-mandated comprehensive clinical assessment of all residents in Medicare- or Medicaid-certified nursing facilities (approximately 96% of US

facilities). It consists of more than 400 items, including sociodemographic information, clinical items (e.g., communication, mood and behavior, signs, symptoms), clinical diagnoses, and treatments provided.[40,65] It includes multi-item summary scales for measures of functional status (ADL Hierarchy Scale),[41,66] cognitive status (Cognitive Performance Scale),[43] and depressed mood (Depression Rating Scale).[42] Nursing staff are required to perform full assessments at admission and annually, as well as reduced assessments on a quarterly basis or after a significant change in resident health.[65] A registered nurse performs the assessment of a resident's status over the previous week based on medical record review, direct observation of and communication with the resident, family interviews, and discussions with the resident's medical and direct care teams.

2.2.2 Study Sample

As shown in **Figure 2-1**, the sampling frame for this study was 166,139 nursing home residents with MDS assessments performed between February 1, 2006, and June 30, 2007. We excluded nursing home residents without a diagnosis of cancer indicated on MDS assessment (n = 142,654); those admitted to the nursing home before February 2006 (n = 13,452); residents whose prescriptions could not be identified using NDCs (n = 1,633); those who were Medicare-ineligible, defined as aged <65 years without ≥1 Medicare-paid prescription drug (n = 25); comatose residents (n = 7); and those missing information on important sociodemographic and clinical characteristics (n = 274). The final sample size was 8,094 residents admitted to 1,382 nursing homes.

2.2.3 Measurement of Pain

Section J of the MDS 2.0 allowed for evaluation of pain, defined as any type of physical pain or discomfort in any part of the body, occurring in the seven days preceding the assessment. The valid[67] and reliable[48] pain-related items address two general characteristics of pain: frequency (no pain, pain less than daily, pain daily) and intensity (mild pain, moderate pain, times when pain is horrible or excruciating (severe)). Nursing staff used a checklist to specify site of pain (e.g., bone, soft tissue). A "skip pattern" allowed the assessor to skip the items on intensity and site of pain if there was no pain present. Instructions for these measures recommended reliance on resident report whenever possible, although staff and family observations, physician records, or medical charts could also have been used.[65] For residents who were unable to communicate, nursing staff were instructed to look for non-verbal cues of pain, such as grimacing or moaning.

2.2.4 Measurement of Analgesic Use

To evaluate the quality of medication use at the beginning of nursing home admission, we identified all drugs dispensed within seven days of a resident's first prescription date. Drug dispensing records were available from February 1, 2006, to June 30, 2007. Data elements included all drugs prescribed and administered to nursing home residents, prescription date, product code (NDC), days' supply, quantity dispensed, and payment source. A database provided by the long-term care pharmacy was used to translate NDCs into therapeutic classes and subclasses.

Opioids are central to existing clinical practice guidelines for management of cancer-related pain. To allow for comparisons with previous work,[6] analgesics were classified into three groups according to the WHO's three-level "ladder" for cancer pain relief.[49] Non-opioids (level 1) included non-steroidal anti-inflammatory drugs and acetaminophen. Aspirin was not considered an analgesic medication because it is typically used among older adults as anti-platelet therapy.[68] Opioids commonly used for mild to moderate pain (level 2) included codeine, hydrocodone, propoxyphene, meperidine, pentazocine, nalbuphine, butorphanol, and any combination of these drugs with level 1 drugs. Opioids commonly used for moderate to severe pain (level 3) included morphine, hydromorphone, oxycodone, buprenorphine, oxymorphone, methadone, levorphanol, and fentanyl. Per more recent clinical practice guidelines that consider pain management by level of opioid-tolerance and alternative modes of administration,[10,50,51] we categorized opioid analgesics by duration of effect (short-acting, long-acting) and by formulation (oral, intravenous/intramuscular, transdermal, suppository). We considered adjuvant medications used for pain management alone or in combination with analgesics. Since indication was absent from drug dispensing records, we identified medication broadly applicable to pain management, including corticosteroids, muscle relaxants, anticonvulsants (i.e., gabapentin, pregabalin), tricyclic antidepressants, selective norepinephrine reuptake inhibitors, alpha-2-adrenergic agonists, transdermal lidocaine, and mexiletine.[68]

2.2.5 Statistical Analysis

We evaluated age trends of resident-level characteristics using likelihood chi-square tests for categorical variables and non-parametric tests (e.g., Kruskal-Wallis test) for continuous variables with skewed distributions. We used multinomial logistic regression models to estimate association among resident characteristics and pain, measured on three levels: daily, less than daily, and none. Binary logistic regression was used to evaluate association among resident characteristics and receipt of analgesics among residents with any pain. To facilitate comparison with published estimates of daily pain and receipt of analgesic medication among nursing home residents with cancer,[6] we performed sensitivity analyses on a reduced study sample of nursing home residents ≥65 years who were admitted to the nursing home from an acute care hospital (n = 6,610). We also separately evaluated receipt of opioid analgesics among nursing home residents with moderate-to-severe pain (n = 3,973).

Regression models were fit using robust estimation of standard errors to account for correlation between residents within the same nursing home.[69] Models were manually constructed in a step-wise fashion. We first evaluated crude associations between each variable and the outcome and, at each stage of model building, selected the strongest variable for inclusion and considered the remaining variables in the presence of those selected for the model. We evaluated correlations among covariates, and if variable pairs were highly collinear (>0.90), only one of the variables was included in the final models. Risk estimates are presented as unadjusted and adjusted ORs and 95% CIs. $P \leq 0.05$ (2-

tailed) was considered statistically significant. All analyses were performed using Stata version 11.2 (StataCorp LP, College Station, TX).

2.3 Results

Newly-admitted nursing home residents had a mean age of 80.0 ± 9.1 years (range: 29.0–105.6 years) and were predominately female (53.1%), non-Hispanic white (83.2%), and admitted from an acute care hospital (86.2%). Nearly 74% and 45% of residents had moderate-to-severe impairment in ADLs and cognition, respectively, with prevalence of both increasing with age ($P<0.001$ for age trend; **Table 2-1**). Similarly, the mean number of medical conditions increased with age ($P<0.001$). Conversely, the prevalence of depressed mood and mean number of medications decreased with age (both $P<0.001$).

2.3.1 Pain

More than 65% of residents with cancer had documented pain, 28.3% had daily pain (95% CI, 27.3–29.2%) and 37.3% had less frequent pain (95% CI, 36.3–38.4%) documented. Daily pain decreased with age ($P<0.001$ for age trend; **Table 2-1**), while less frequent pain increased with age ($P<0.001$). Clinical conditions potentially associated with pain, including arthritis, osteoporosis, and hip fractures, were more prevalent with increasing age ($P<0.001$).

Compared to residents aged 65–74 years, older residents were less likely to have pain documented on a daily basis or less (**Table 2-2**). Independent of age, those with cognitive impairment, feeding tubes, or who were restrained were less likely to have

daily pain recorded. Conversely, women, residents admitted from a hospital, those with compromised ADLs, depressed mood, an indwelling catheter or an explicit terminal prognosis, or who were bedfast had increased odds of pain. Results were consistent in sensitivity analysis of nursing home residents ≥65 years admitted from a hospital (**Table A-1**); however, non-Hispanic blacks were less likely than non-Hispanic whites to have documented pain.

2.3.2 Receipt of Analgesics

Analgesics comprised 9.5% of medications dispensed within the first week of nursing home admission. More than half of nursing home residents (58.8%) received an analgesic (mean 1.8 ± 0.9, range: 1–8). Nearly 12% received at least one non-opioid, 46.6% at least one level 2 drug, and 15.3% at least one level 3 drug. Specifically, 51.5% received a level 2 drug only, 7.7% received a non-opioid only, and 9.6% received a level 3 drug only. One-fifth received multiple analgesics of varying strength according to the WHO three-level ladder (7.1% received a non-opioid plus a level 2 drug; 1.4%, a non-opioid plus a level 3 drug; 10.9%, a level 2 drug plus a level 3 drug; and 1.4%, all three). Hydrocodone was the most commonly prescribed analgesic (comprising 26.7% of analgesic prescriptions), followed by oxycodone (19.1%), fentanyl (9.1%), and propoxyphene (8.9%, withdrawn from the US market in 2010[33]). Approximately 36% of residents with daily severe pain and 21% of residents with daily moderate pain used long-acting opioids (**Table 2-3**).

Overall, 27.6% of nursing home residents with documented pain received no analgesics (95% CI: 26.4–28.9%). Among those in daily pain, 17.5% received no analgesics (95% CI: 16.0–19.1%), including 11.7% whose daily pain was severe (95% CI: 8.9–14.5%) and 16.9% whose daily pain was moderate (95% CI: 15.1–18.8%). More than 35% of residents with less frequent pain did not receive treatment (95% CI: 33.6–37.0%), including 21.5% with severe pain (95% CI: 15.8–27.1%) and 28.3% with moderate pain (95% CI: 26.2–30.4%). There were no differences by pain severity with respect to problems swallowing (P=0.185), but those with moderate pain were more likely than those with mild or with severe pain to have medication restrictions documented in their medical record (P <0.001). Those with untreated pain were less likely than those with treated pain to receive an adjuvant medication (17.2% vs. 25.0%, P<0.001).

Relative to residents aged 65–74 years, older residents were less likely to receive analgesics for their pain, although the 95% CI included unity for those aged 75–84 years (**Table 2-4**). Similarly, those with cognitive impairment, feeding tubes, and restraints were less likely to receive analgesics. Conversely, women were more likely than men to receive treatment. Receipt of analgesics was also positively associated with nursing home admission from a hospital, increasing number of non-analgesic medications, and terminal prognosis. Results were generally consistent in sensitivity analyses of older nursing home residents admitted from a hospital (**Table A-2**) and of nursing home residents in moderate-to-severe pain (**Table A-3**). However, the latter sensitivity analysis did not find

a statistically significant association of opioid treatment among women and residents who used restraints.

2.4 Discussion

This study reveals that the majority (65.6%) of nursing home residents with a cancer diagnosis experience pain. A substantial proportion of that pain is daily, and moderate to severe in intensity. Between 2006 and 2007, 17.6% of nursing home residents with daily pain lacked treatment with analgesics in the first week of nursing home admission. These results are only modestly decreased from those documented before national efforts to improve the quality of pain management in nursing homes.

Between 1992 and 1995, approximately 26% of nursing home residents in daily pain did not receive any analgesic agent.[6] Earlier estimates of medication receipt may be underreported due to a reliance on pharmacist- and nurse-reported medication lists (Section U of the MDS). Our use of long-term care pharmacy dispensing records offers improved identification of analgesic treatment. Because Section U was removed from the MDS, we were unable to disentangle the extent to which the observed improvement in pain management may be an artifact of differences in measurement methodology rather than a true shift in practice patterns.

We anticipated improvements in pain management since the mid-1990s for several reasons. The CMS nursing home quality indicators focused on pain were tested beginning in 1998,[70] and public reporting of the prevalence of uncontrolled pain began in 2002.[60] Thirteen states have passed or updated legislation since 1998 to improve access to

scheduled drugs for treatment of intractable pain.[71] In addition, the Federation of State Medical Boards published their *Policy on the Use of Opioid Analgesics in the Treatment of Chronic Pain* encouraging the adequate treatment of patients in pain and appropriate use of opioids,[72] and nearly 30 states have adopted the *Policy* for their own policies. Despite these efforts, untreated pain remains a significant problem among nursing home residents with cancer.

Further, among this medically-needy patient population, a number of particularly vulnerable sub-groups continue to be at higher risk of having their pain go untreated. Consistent with previous findings,[6,33,34] we found that the oldest old and those with cognitive impairment were more likely to not receive treatment for their documented pain. Despite the widespread dissemination of clinical guidelines for pain management in older adults, adequate pain management among older adults may be complicated by the presence of comorbid conditions, increased risk of adverse effects, and physician factors such as inadequate training or reluctance to prescribe opioids.[73] Cognitive impairment may preclude nursing home residents from effectively communicating their need for pain relief. Although nursing staff have detailed instructions on pain assessment in non-verbal residents,[65] providers may continue to rely on patients' verbal reports when deciding to treat pain.[74] Indeed, even in our sensitivity analysis of nursing home residents with documented moderate-to-severe pain, those with cognitive impairment were less likely to receive analgesic medication.

Facility-level characteristics have been shown to impact quality of pain management among nursing home residents. For example, residents whose cancer was

diagnosed after nursing home admission were less likely to receive pain medication in facilities with a high Medicaid patient load or with a higher Medicare-paid percentage of days.[75] While it was beyond the scope of this study to evaluate organizational factors related to receipt of analgesics, we found that nursing home residents with feeding tubes or restraints—devices known to be associated with poor nursing home quality[76,77]—had decreased odds of receiving analgesics for their documented pain. This study provides additional evidence that nursing home quality is associated with quality of care provided to residents.

The present study has several strengths worth highlighting. First, it is a much-needed update to what is already known about pain management among nursing home residents with cancer. While our evaluation of daily pain permits comparisons with previous research, we also provide new evidence around more nuanced facets of pain, including pain intensity and the prevalence and treatment of infrequent pain. Second, we provide new evidence on pain management that is relevant to a broader population of nursing home residents with cancer. Indeed, study participants were drawn from a national sample of nursing homes across 46 states and were admitted to the nursing home from both acute and non-acute settings. Third, data were from newly-admitted nursing home residents and thus permitted evaluation of medication quality at the beginning of a nursing home stay. Fourth, we used a unique prescription dispensing data source that spanned all payers (i.e., Medicare Parts A/B, Medicare Part D, Medicaid, third party private insurance, cash, and facility/hospice) and thus represented all types of nursing home residents. Previous studies of analgesic medication use in nursing homes have

examined only beneficiaries of single-payer sources.[31,32] Finally, our data source included over-the-counter as well as prescription medications dispensed to nursing home residents during the study period, allowing for prevalence estimates of non-opioid analgesics.

There were also some limitations. We reference the WHO analgesic ladder, which has been subject to numerous debate and criticism[78–81] owing to its omission of alternative routes of drug administration, nonpharmaceutical treatments, and interventional procedures. Despite these limitations, the WHO analgesic ladder has demonstrated effectiveness and widespread utility, and remains the reference point for cancer-related pain management.[50,51] This was a cross-sectional study of pain management in the first week of nursing home admission, a period of great transition during which care processes may suffer. While we cannot comment on the quality of pain management among residents with longer nursing home stays, previous research has shown that more than half of cancer patients with pain have severe pain on subsequent quarterly MDS assessment.[5] Although MDS 2.0 pain assessments could be augmented by nursing staff and family observations, concerns remain about potential misclassification of pain, especially among residents with difficulty communicating. Although we considered a resident's pain to be treated if they had at least one dispensing record for an analgesic, we were unable to determine whether the treatment provided adequate pain relief. Therefore, our results may underestimate the true prevalence of pain and its treatment. We also acknowledge that it is possible that pain medications started before admission to the nursing home were not re-evaluated. We were not able to definitively attribute cancer as the underlying pathology of pain, nor were we able to specify cancer

type. However, guidelines on the use of analgesic medication for persistent pain among older adults are not cancer-specific. Although we provide prevalence estimates of adjuvant medication use, we were unable to evaluate non-pharmacological approaches to pain management owing to the absence of this information in the MDS 2.0. Future studies using the MDS 3.0 may be better able to evaluate these alternative approaches to pain management. Finally, dispensing records lacked the indication for medication use and information on medications used prior to nursing home admission, so we could not determine appropriateness of treatment.

2.5 Conclusion

This study contributes a much-needed update on the quality of pain management among nursing home residents with cancer, a critical public health issue of increasing prominence. Pain remains common and undertreated among some of the most vulnerable cancer patients in the US, and special attention should be paid to the oldest old, those with cognitive impairment, and residents of potentially poor quality nursing homes. Among nursing home residents overall, recent national goals for prevalence of moderate-to-severe pain were 15% for short-stay, post-acute residents and 4% for long-stay residents.[82] Although cancer-specific targets for pain management do not currently exist, these data suggest that the current state of pain management among nursing home residents with cancer falls short of these goals. New information provided here may provide initial directions for targeted efforts to improve the quality of pain treatment in

nursing homes, including redoubled efforts to disseminate older adult-specific clinical practice guidelines in this setting.

Figure 2-1: Sample Selection Strategy

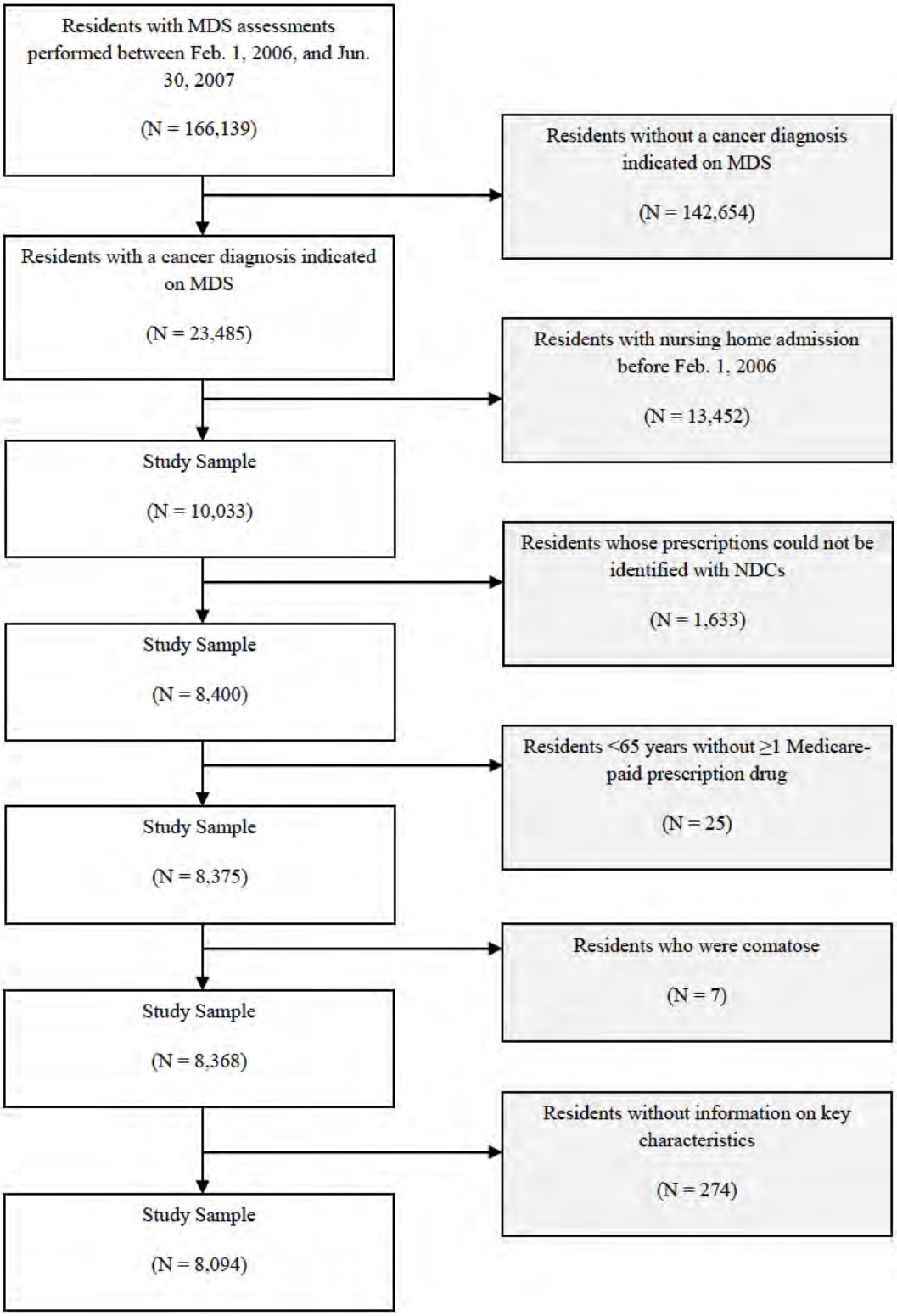


Table 2-1: Characteristics of Newly Admitted Nursing Home Residents with Cancer, by Age Group

	<65 years n = 421	65–74 years n = 1,682	75–84 years n = 3,459	≥85 years n = 2,532
Women	56.3	52.7	51.1	55.6
Race and ethnicity				
Non-Hispanic white	73.4	76.5	83.7	88.7
Non-Hispanic black	18.8	15.6	10.2	6.8
Hispanic	4.0	5.6	4.0	3.0
Asian or Pacific Islander	3.1	2.1	2.0	1.3
American Indian or Alaskan Native	0.7	0.2	0.1	0.2
Source of admission				
Acute care hospital	86.9	89.8	87.2	82.4
Private home	4.8	4.4	6.2	8.2
Other nursing home	4.5	3.0	3.8	5.2
Other[a]	3.8	2.8	2.9	4.3
Widowed	12.1	28.5	42.1	62.4
Degree of functional impairment[b]				
Moderate	39.9	44.5	49.3	49.0
Severe	27.1	27.2	26.0	26.7
Degree of cognitive impairment[c]				
Moderate	24.0	29.3	40.5	50.8
Severe	4.3	3.2	4.3	4.9
Depressed mood[d]	13.8	9.0	7.8	7.6
Bedfast	5.5	5.8	4.6	3.7
Terminal prognosis[e]	8.3	8.9	8.4	7.3
Number of diagnoses	5.5 ± 2.6 (1–15)	5.7 ± 2.5 (1–19)	6.1 ± 2.5 (1–16)	6.2 ± 2.4 (1–16)
Clinical conditions				
Arthritis	12.6	18.4	22.8	27.6

	<65 years n = 421	65–74 years n = 1,682	75–84 years n = 3,459	≥85 years n = 2,532
Osteoporosis	4.8	8.2	11.7	15.3
Hip fracture	3.3	5.3	6.6	9.3
Number of medications in first week	11.1 ± 5.7 (1–35)	9.9 ± 5.4 (1–35)	9.2 ± 4.9 (1–33)	7.9 ± 4.5 (1–31)
Number of non-analgesics in first week	9.9 ± 5.4 (0–34)	8.9 ± 5.1 (0–34)	8.3 ± 4.7 (0–32)	7.2 ± 4.2 (0–28)
Pain frequency[f]				
Daily	43.2	35.1	28.0	21.7
Less than daily	33.5	37.0	37.6	37.8

N = 8,094

Percentage or mean ± standard deviation (range) shown

[a] Includes board and care/assisted living/group home, psychiatric hospital, rehabilitation hospital.

[b] Based on 7-level scale: Activities of Daily Living Hierarchy Scale score of 3 or 4 for moderate impairment, 5 or 6 for severe impairment.[41]

[c] Based on 7-level scale: Cognitive Performance Scale score of 2 to 4 for moderate impairment, 5 or 6 for severe impairment.[43]

[d] Based on a scale from 0–14: Depression Rating Scale scores of 3 or more indicate major or minor depressive disorders.[42]

[e] Indicated by prognosis of <6 months or receipt of hospice.

[f] As assessed by nursing home staff over a 7-day period.

Table 2-2: Correlates of Pain in Newly Admitted Nursing Home Residents with Cancer

	Pain frequency			Daily pain vs. no pain (referent)		< Daily pain vs. no pain (referent)	
	Daily n = 2,291	< Daily n = 3,022	None n = 2,781	Unadjusted OR (95% CI)	Adjusted[a] OR (95% CI)	Unadjusted OR (95% CI)	Adjusted[a] OR (95% CI)
Age, years							
<65	7.9	4.7	3.5	1.48 (1.11–1.96)	1.45 (1.08–1.95)	1.08 (0.82–1.42)	1.11 (0.85–1.46)
65–74	25.8	20.6	16.9	Referent	Referent	Referent	Referent
75–84	42.3	43.1	42.7	0.65 (0.56–0.75)	0.70 (0.60–0.82)	0.83 (0.72–0.94)	0.86 (0.74–0.99)
≥85	24.0	31.6	36.9	0.42 (0.36–0.50)	0.48(0.41–0.58)	0.70 (0.60–0.81)	0.75 (0.63–0.88)
Women	59.8	54.5	46.1	1.74 (1.54–1.95)	1.67 (1.46–1.91)	1.40 (1.26–1.55)	1.35 (1.20–1.51)
Race and ethnicity							
Non-Hispanic white	83.9	83.9	82.0	Referent	Referent	Referent	Referent
Non-Hispanic Black	10.6	9.8	11.8	0.87 (0.73–1.05)	0.87 (0.73–1.05)	0.81 (0.66–0.98)	0.82 (0.67–1.01)
Hispanic	3.9	4.3	3.9	0.98 (0.73–1.32)	1.01 (0.75–1.37)	1.08 (0.82–1.40)	1.06 (0.81–1.39)
Asian or Pacific Islander	1.4	1.9	2.1	0.66 (0.46–0.95)	0.70 (0.49–1.01)	0.87 (0.56–1.35)	0.85 (0.57–1.26)
American Indian or Alaskan Native	0.2	0.2	0.1	1.48 (0.40–5.55)	1.60 (0.49–5.21)	1.58 (0.46–5.41)	1.49 (0.41–5.41)
Admitted from acute hospital	88.2	87.9	82.7	1.56(1.32–1.84)	1.52 (1.27–1.82)	1.52 (1.30–1.77)	1.44 (1.23–1.69)
Widowed	42.7	45.7	43.6	0.96 (0.86–1.08)	1.02 (0.89–1.17)	1.09 (0.98–1.21)	1.08 (0.96–1.22)
Functional impairment[b]	76.0	74.6	72.6	1.19 (1.04–1.37)	1.33 (1.15–1.54)	1.11 (0.98–1.26)	1.16(1.01–1.32)
Cognitive impairment[c]	35.9	44.0	53.0	0.50 (0.44–0.56)	0.62 (0.54–0.72)	0.70 (0.62–0.78)	0.78 (0.69–0.89)

	Pain frequency			Daily pain vs. no pain (referent)		< Daily pain vs. no pain (referent)	
	Daily n = 2,291	**< Daily n = 3,022**	**None n = 2,781**	**Unadjusted OR (95% CI)**	**Adjusted[a] OR (95% CI)**	**Unadjusted OR (95% CI)**	**Adjusted[a] OR (95% CI)**
Depressed mood[d]	12.1	7.7	5.7	2.28 (1.82–2.84)	2.27 (1.79–2.88)	1.37 (1.11–1.70)	1.46 (1.16–1.83)
Feeding tubes	5.0	7.9	7.5	0.65 (0.52–0.82)	0.64 (0.50–0.82)	1.06 (0.87–1.29)	1.10 (0.90–1.37)
Indwelling catheter	27.1	24.1	19.1	1.58 (1.39–1.80)	1.52 (1.32–1.75)	1.35 (1.19–1.53)	1.28 (1.12–1.46)
Use of restraints[e]	0.9	1.8	2.7	0.34 (0.20–0.56)	0.50 (0.30–0.86)	0.67 (0.47–0.94)	0.81 (0.57–1.16)
Bedfast	6.7	4.4	3.1	2.23 (1.70–2.93)	2.06 (1.54–2.74)	1.41 (1.07–1.86)	1.37 (1.02–1.83)
Terminal prognosis[f]	11.3	7.9	5.8	2.06 (1.65–2.57)	2.21 (1.73–2.83)	1.39 (1.12–1.72)	1.58 (1.26–1.98)

N = 8,094

CI: confidence interval; **OR:** odds ratio

[a] Adjusted for all variables listed in Table 2-1 and variables describing participation in Minimum Data Set assessment (resident, family, significant other) and communication skills.

[b] Activities of Daily Living Hierarchy Scale scores equal 3 or more.[41]

[c] Cognitive Performance Scale scores equal 2 or more.[43]

[d] Depression Rating Scale scores equal 3 or more.[42]

[e] Includes trunk and limb restraints as well as chairs to prevent rising.

[f] Indicated by prognosis of <6 months or receipt of hospice.

Table 2-3: Use of Any Analgesic Medication in First Week of Nursing Home Admission in Residents with Cancer and Any Pain, by Pain Intensity and Frequency[a]

Pain intensity	Pain frequency	
	Daily	**< Daily**
Severe pain	n = 512	n = 205
No analgesic	11.7	21.5
Any analgesic	88.3	78.5
Level 1 drug only[b]	1.0	4.9
Level 2 drug only[c]	37.3	40.5
Level 3 drug only[d]	16.8	12.7
Level 1 + Level 2	4.5	5.9
Level 1 + Level 3	2.7	1.0
Level 2 + Level 3	23.4	11.2
All	2.5	2.4
Adjuvant[e]	25.6	25.4
Duration of effect (opioids only)		
Short-acting	80.9	71.2
Long-acting	35.7	17.1
Formulation (opioids only)		
Oral	83.8	71.7
Non-oral[f]	25.8	13.7
Transdermal	23.2	12.2
Intravenous or intramuscular	4.9	2.0
Moderate pain	n = 1,536	n = 1,720
No analgesic	16.9	28.3
Any analgesic	83.1	71.7
Level 1 drug only[b]	2.9	3.4
Level 2 drug only[c]	48.7	45.7
Level 3 drug only[d]	9.2	6.5
Level 1 + Level 2	6.6	6.2
Level 1 + Level 3	1.1	1.2
Level 2 + Level 3	13.2	7.6
All	1.4	1.1
Adjuvant[e]	25.7	21.4
Duration of effect (opioids only)		
Short-acting	75.1	64.8
Long-acting	21.1	12.4
Formulation (opioids only)		

Pain intensity	Pain frequency	
	Daily	**< Daily**
Oral	78.3	66.0
Non-oral[f]	14.8	9.7
Transdermal	13.5	8.3
Intravenous or intramuscular	1.7	1.4
Mild pain	n = 243	n = 1095
No analgesic	33.7	48.9
Any analgesic	66.3	51.1
Level 1 drug only[b]	4.9	9.3
Level 2 drug only[c]	39.1	28.5
Level 3 drug only[d]	3.7	4.2
Level 1 + Level 2	8.2	4.7
Level 1 + Level 3	1.6	0.5
Level 2 + Level 3	6.6	3.4
All	2.1	0.5
Adjuvant[e]	23.5	19.3
Duration of effect (opioids only)		
Short-acting	59.3	39.5
Long-acting	9.9	5.4
Formulation (opioids only)		
Oral	60.9	39.5
Non-oral[f]	7.0	4.8
Transdermal	5.8	4.0
Intravenous or intramuscular	1.2	1.0

N = 5,311

Percentages presented may not add to 100% due to rounding.

[a] Of 5,313 nursing home residents with any pain, 2 have missing pain intensity data.

[b] Classified by the World Health Organization as a level 1 drug, including non-steroidal anti-inflammatory drugs and acetaminophen.

[c] Includes codeine, hydrocodone, propoxyphene, meperidine, pentazocine, nalbuphine, butorphanol, and any combination of these drugs with level 1 drugs.

[d] Includes morphine, oxycodone, buprenorphine, hydromorphone, oxymorphone, methadone, levorphanol, and fentanyl.

[e] Includes corticosteroids, muscle relaxants, anticonvulsants, tricyclic antidepressants, selective norepinephrine reuptake inhibitors, alpha-2-adrenergic agonists, transdermal lidocaine and mexiletine.[26]

[f] Suppository opioid formulations were used by <0.1% of the study population.

Table 2-4: Correlates of Receiving Any Analgesic in Newly Admitted Nursing Home Residents with Cancer and Any Pain

	Any analgesic n = 3,844	No analgesic n = 1,469	Likelihood of receiving any analgesic for any pain	
			Unadjusted OR (95% CI)	Adjusted[a] OR (95% CI)
Age				
<65	7.0	3.8	1.41 (1.02–1.95)	1.33 (0.96–1.85)
65–74	24.4	18.9	Referent	Referent
75–84	43.2	41.6	0.80 (0.68–0.95)	0.88 (0.74–1.04)
≥85	25.5	35.7	0.55 (0.47–0.66)	0.67 (0.55–0.81)
Women	57.6	54.6	1.13 (1.00–1.28)	1.16 (1.02–1.33)
Race and ethnicity				
Non-Hispanic white	84.4	82.5	Referent	Referent
Non-Hispanic black	9.8	11.0	0.87 (0.72–1.06)	0.85 (0.69–1.05)
Other	5.8	6.5	0.87 (0.68–1.11)	0.81 (0.62–1.05)
Admitted from acute care hospital	88.8	86.1	1.29 (1.08–1.54)	1.25 (1.03–1.51)
# other medication in first week				
≤5	25.0	45.2	Referent	Referent
6–10	40.2	32.7	2.22 (1.91–2.59)	2.46 (2.12–2.86)
≥11	34.8	22.1	2.86 (2.41–3.39)	3.13 (2.64–3.72)
Functional impairment[c]	75.1	75.5	0.98 (0.85–1.13)	1.13 (0.97–1.32)
Cognitive impairment[d]	37.1	49.4	0.60 (0.53–0.68)	0.71 (0.61–0.82)
Depressed mood[e]	10.1	8.4	1.23 (0.99–1.52)	1.26 (1.00–1.58)
Feeding tubes	6.4	7.4	0.85 (0.68–1.06)	0.77 (0.60–0.99)
Use of restraints[f]	1.0	2.4	0.43 (0.28–0.67)	0.50 (0.31–0.82)
Bedfast	5.6	4.8	1.19 (0.89–1.59)	1.19 (0.88–1.61)
Terminal prognosis[g]	9.8	8.4	1.18 (0.95–1.48)	1.45 (1.14–1.80)

N = 5,313; percentages presented.
CI: confidence interval; **OR:** odds ratio
[a] Adjusted for all variables listed in Table 2-1 and variables describing participation in MDS assessment (family, significant other) and communication skills.
[b] Includes Hispanic, Asian or Pacific Islander, American Indian or Alaskan Native.
[c] Activities of Daily Living Hierarchy Scale scores equal 3 or more.[41]
[d] Cognitive Performance Scale scores equal 2 or more.[43]
[e] Depression Rating Scale scores equal 3 or more.[42]
[f] Includes trunk and limb restraints as well as chairs to prevent rising.
[g] Indicated by prognosis of <6 months or receipt of hospice.

CHAPTER III:

SHOULD OPIOID PAIN MEDICATIONS RECEIVE SPECIAL MEDICARE PART D COVERAGE PROTECTION FOR NURSING HOME RESIDENTS WITH CANCER?

ABSTRACT

Background: Fentanyl patches are commonly employed to treat nursing home residents with intractable cancer pain. However, access to fentanyl patches—among the strongest and most expensive of opioid formulations—may have been affected by coverage restrictions of Medicare Part D, the leading source of prescription drug coverage in nursing homes. Our objective was to evaluate Medicare Part D's impact on use of fentanyl patches and use of less costly or less effective opioid analgesics among nursing home residents with cancer.

Methods: This quasi-experimental study included 18,599 Medicare-eligible residents with cancer admitted to 1,112 nursing homes. We used data from the MDS 2.0 linked to all-payer long-term care pharmacy dispensing records (January 2005-June 2007) to estimate changes in receipt of fentanyl patches, other strong opioids, and weak opioids after Medicare Part D implementation. For each drug category, we calculated monthly proportions of residents receiving $\geq$1 prescription and therapy days covered. Segmented Poisson regression estimated immediate and trend changes in medication use after Medicare Part D, adjusting for baseline trends.

Results: We observed increasing trends for all opioid drug categories prior to Medicare Part D. After Medicare Part D, receipt of fentanyl patches and other strong opioids abruptly decreased by 10% and 21%, respectively. Residents with cancer were less likely to receive fentanyl patches after Medicare Part D relative to historical trends (IRR = 0.98; P<0.001), but more likely to receive other strong opioids (IRR, 1.01; P = 0.02). Trends in weak opioids remained unchanged.

Conclusions: We observed immediate and sustained reductions in the receipt of fentanyl patches and other opioids among nursing home residents with cancer after implementation of Medicare Part D. Although the clinical impact of these patterns is uncertain, this finding suggests cost-related barriers to therapeutic options in the treatment of cancer pain in nursing homes.

3.1 Introduction

Since 2006, Medicare Part D has been the leading source of prescription drug coverage for older adults. Under this benefit, medications fall into protected or excluded drug classes, or neither. Participating private prescription drug plans must include in their formularies "all or substantially all" drugs and unique dosage forms within six protected classes of medical concern: antineoplastics, antidepressants, antipsychotics, anticonvulsants, antiretrovirals, and immunosuppressants.[11] In addition, for beneficiaries taking a specific medication within a protected drug class, plans are prohibited from employing utilization management requirements (e.g., prior authorization, step therapy) that would otherwise steer beneficiaries to preferred alternatives. Conversely, plans cannot cover medications excluded under basic Medicare Part D coverage (e.g., benzodiazepines, nonprescription drugs, vitamins and minerals). Formularies must include at least two chemically distinct drugs within the classes that are neither protected nor excluded.[11] Given the absence of other Medicare Part D guidance on these drug classes, individual plans have flexibility in selecting the particular drugs covered and employing utilization management requirements.

There is evidence that Medicare Part D's exclusion of benzodiazepines led to disruptions in medication use and some substitutions with other psychotropic drugs.[38,83–85] Similar patterns of disruption have been observed in the nursing home setting among angiotensin receptor blockers, cholinesterase inhibitors, and long-acting opioids, which are medications that are neither protected nor excluded.[86] However, the impact of

Medicare Part D on these and other classes of unprotected medications is not well understood.

Data regarding impact of Medicare Part D on opioid use, in particular, are scant. Fentanyl, a potent, synthetic opioid analgesic, is indicated for persistent, moderate to severe pain in opioid-tolerant patients.[7] Despite FDA public health advisories of life-threatening side effects when used as initial therapy,[87] transdermal fentanyl systems (patches) that deliver analgesia over a 72-hour period remain an important mainstay of analgesic therapy for older adults.[88] Because of concerns about inappropriate opioid use among Medicare beneficiaries,[36] Medicare Part D plans may more readily employ coverage restrictions or utilization management strategies to reduce opioid use. Consequently, during the first year of Medicare Part D, 66% of claims for fentanyl patch were not reimbursed because of non-coverage.[37] Four years later, utilization management requirements and administrative rejections (e.g., inadequate justification for a prescription order) accounted for 99% of non-reimbursed claims.[13]

The nursing home setting provides a unique context to study the effect of Medicare Part D on a vulnerable population – older adults with cancer. As the provision of continuing care for older adults has shifted away from the acute care setting, nursing homes have become an increasingly essential provider of cancer care for those with complex health needs. Among an estimated 1.4 million nursing home residents,[4] 8.8% have a cancer diagnosis that affects their function or treatment.[5] One-third of Medicare beneficiaries with cancer receive nursing home care during the last 90 days of life, and 17.1% die in this setting.[30] Pain is the most common cancer symptom in older adults and

is prevalent in long-term care settings, with up to 29.4% of nursing home residents with cancer experiencing pain on a daily basis.[6,89] Opioids are the mainstay of cancer pain management because of their effectiveness in controlling moderate to severe pain and are the most frequently used analgesics in nursing homes.[12] We previously found that fentanyl accounted for 9.1% of all analgesics prescribed to nursing home residents with cancer in 2006 to 2007.[89] Fentanyl patches are more expensive than oral opioids of similar strength; a single 50 mcg/hr film costs between $14.10 and $22.85.[90] Coupled with a legal obligation for nursing homes to provide all prescription drugs required by residents' care plans, fentanyl patches may be especially costly for nursing homes to provide to residents.[91] Medicare Part D coverage restrictions may have further affected nursing home residents' access to fentanyl patches.

We used a quasi-experimental research design to examine the relationship between Medicare Part D implementation and changes in fentanyl patch use among more than 18,500 nursing home residents with cancer. Given the safety and cost-related concerns surrounding fentanyl patch use, we hypothesized that Medicare Part D led to an immediate reduction in use of fentanyl patches. To assess substitution in analgesic medication use, we also evaluated concomitant changes in prevalence of other strong opioids and less potent opioids.

3.2 Methods

The institutional review board of the University of Massachusetts Medical School approved this study.

3.2.1 Data Source

Data were provided by a large long-term care pharmacy and come from more than 2.5 million unique individuals living in nearly 16,000 nursing homes in 48 states. Data include nursing home resident health assessments from the MDS version 2.0 linked with an all-payer administrative data source of all dispensed prescription and over-the-counter medication.

3.2.2 Study Sample

As shown in **Figure 3-1**, the sampling frame for this study was 234,308 nursing home residents with MDS assessments performed between January 1, 2005, and June 30, 2007. We excluded nursing home residents without a cancer diagnosis indicated on any MDS assessment (n = 210,823); residents who were ineligible for Medicare (i.e., <65 years with no evidence of a Medicare-paid medication) at any point during the study (n = 1,320); residents missing information on important sociodemographic and clinical characteristics (n = 1,183); and residents in facilities that lacked pharmacy dispensing records in both pre- and post-Medicare Part D periods (n = 2,383). The final sample size was 18,599 nursing home residents with cancer who were admitted to 1,112 facilities

nationwide and generated 1,591,067 prescription records from January 2005 through June 2007.

3.2.3 Measurement of Analgesic Use

Dispensing records were available from January 1, 2005 to June 30, 2007. Data elements included all prescription and over-the-counter medication dispensed to nursing home residents, dispensing date, product code (NDC), days' supply, quantity dispensed, and payment source. We used a database provided by the long-term care pharmacy to translate NDCs into therapeutic classes and subclasses.

We created four categories of analgesics: 1) all opioids typically used to treat moderate to severe pain (WHO level 3 drugs); 2) fentanyl patches; 3) potential fentanyl substitutes (other WHO level 3 drugs); and 4) opioids used for mild to moderate pain (WHO level 2 drugs). Fentanyl patches included branded and generic medications. Other WHO level 3 drugs included oral and injectable formulations of fentanyl, morphine, hydromorphone, oxycodone, oxymorphone, methadone, buprenorphine, and meperidine.[49] Level 2 drugs included codeine, hydrocodone, propoxyphene, pentazocine, butorphanol, standardized opium, tramadol, and any combination of these drugs with non-steroidal anti-inflammatory drugs and acetaminophen.[49] For each of the four categories of analgesics, we created two measures: 1) monthly proportion of nursing home residents receiving ≥1 prescription of interest and 2) monthly proportion of resident-therapy days covered.

3.2.4 Statistical Analysis

We conducted descriptive analyses comparing nursing home resident characteristics and source of payment for fentanyl patch prescriptions prior to and after the implementation of Medicare Part D. Previous analyses of the data showed uneven capture of payment sources for the first month of the Medicare Part D program (January 2006),[92] so estimates for this month are not reported here. Prescribing rates of all WHO level 3 drugs, fentanyl patches, other WHO level 3 drugs, and WHO level 2 drugs were graphically examined during each month from January 2005 through December 2005 (pre-Medicare Part D implementation) and from February 2006 through June 2007 (post-Medicare Part D implementation). We evaluated the linearity of the relationship between prescribing rates and time within each of the two time segments and, based on the visual inspection of the prescribing rates, decided to fit a Poisson model, which is appropriate for counts of rare events.[56] We develop a segmented regression model using a generalized linear model approach to estimate the immediate change in the prescribing rate level and the gradual change in trend after the implementation of Medicare Part D.[55] The basic model includes a constant summarizing the baseline level and three terms. The first term estimates monthly changes per nursing home resident in the period before Medicare Part D implementation, the second estimates the average level change per nursing home resident in the first month after Medicare Part D implementation, and the third is the trend after Medicare Part D relative to the trend before Medicare Part D implementation. The sum of the first and third terms represents monthly changes per resident in the post-Medicare Part D implementation period. We adjusted this model for underlying time

trend (a continuous variable for each month) and rates for January 2006 (a dummy variable for this transition month). We also evaluated and ruled out seasonal effect (dummy variables for quarters in each calendar year). The impact of Medicare Part D on medication use might differ in vulnerable populations. We therefore performed sensitivity analyses in the subset of beneficiaries who were dually eligible for Medicare and Medicaid (n = 4,266).

Segmented regression models were fit using Newey-West standard errors to account for possible serial correlation of consecutive observations.[59] Risk estimates are presented as adjusted IRRs and 95% CIs. $P \leq 0.05$ (two-tailed) was considered statistically significant. All analyses were performed using Stata version 11.2 (StataCorp LP, College Station, TX).

3.3 Results

A comparison of resident sociodemographic and clinical characteristics before and after the January 2006 implementation of Medicare Part D showed few differences between nursing home residents in the two time periods (**Table 3-1**). Explicit terminal prognosis was more prevalent prior to the policy change (9.7% pre-implementation vs. 7.8% post-implementation, $P<0.001$), as was severe impairment in ADLs (27.0% vs. 24.6%, $P<0.001$). However, documented pain was more prevalent after Medicare Part D implementation relative to the pre-Medicare Part D period (58.4% vs. 55.9%, $P<0.001$).

3.3.1 Source of Payment for Fentanyl Patches

Prior to Medicare Part D, fentanyl patches represented 1.3% (n = 7,302) of all dispensed prescriptions and were paid by Medicare Parts A/B (33.3% of prescriptions), Medicaid (29.6%), third party insurance (23.1%), facility/hospice (9.3%), and cash (4.7%). As in 2005, fentanyl patches represented 1.3% (n = 11.349) of all dispensed prescriptions after implementation of Medicare Part. However, Medicare Part D became the leading payer of fentanyl patches (46.5%), followed by Medicare Parts A/B (24.9%), third party insurance (13.7%), facility/hospice (7.7%), cash (4.8%), and Medicaid (2.3%).

Similarly, among dual-eligible beneficiaries, fentanyl patches represented 1.3% of all dispensed prescriptions in each of the two time periods. In 2005, prescriptions were paid by Medicaid (49.6%), third party insurance (25.7%), Medicare Parts A/B (14.8%), facility/hospice (7.7%), and cash (2.2%). After February 2006, Medicare Part D became the leading payer for fentanyl patch prescriptions (68.5%), followed by third party insurance (11.6%), Medicare Parts A/B (7.6%), facility/hospice (6.1%), cash (3.4%), and Medicaid (2.9%).

3.3.2 Effect of the 2006 Implementation of Medicare Part D

Figure 3-2 displays the differential effects of Medicare Part D by drug category (Panels A-D). Rate of nursing home residents receiving medication (per 1,000 residents) is shown in the left column. Rate of therapy days covered (per 1,000 resident-therapy days) is shown in the right column. Actual monthly rates are shown as bullet points before and after Medicare Part D implementation, which is represented by the dashed

vertical line at month 12. Solid lines represent the pre- and post-Medicare Part D slopes, while dashed lines represent the expected slope had Medicare Part D not been implemented. **Table 3-2** provides risk estimates of the effects of Medicare Part D by drug category.

Prior to Medicare Part D, the monthly rate of medication recipients and monthly rate of therapy days covered appeared to increase for all WHO level 3 drugs (**Figure 3-2A**), including fentanyl patches (**Figure 3-2B**) and other WHO level 3 drugs (**Figure 3-2C**), as well as WHO level 2 drugs (**Figure 3-2D**). The models demonstrate that the rate of all WHO level 3 drug receipt increased 2.0% per month, while the rate of therapy days covered increased 1.0% per month in 2005. Rate of fentanyl patch receipt also increased 2.0% per month, but rate of therapy days covered was steeper than that of WHO level 3 drugs overall: 4.0% per month. While the rate of receipt of other WHO level 3 drugs increased 1.0% per month, the monthly rate of therapy days covered was unchanged throughout 2005. Similarly, the rate of receipt of WHO level 2 drugs increased 1.0% per month, while the rate of therapy days covered was unchanged.

In the first month after Medicare Part D implementation, all WHO level 3 drug categories experienced marked decreases in rate of medication receipt and rate of therapy days covered. Among all WHO level 3 drugs, rate of medication receipt decreased by 13.0% (95% CI: 11.0–17.0%) and rate of therapy days covered decreased by 26.0% (95% CI: 23.0–28.0%). The rate of receipt of fentanyl patches decreased by 10.0% (95% CI: 7.0–13.0%) and rate of therapy days covered decreased by 22.0% (95% CI: 16.0–28.0%). Similarly, the rate of receipt of other WHO level 3 drugs decreased by 21.0% (95% CI:

16.0–25.0%) and rate of therapy days covered decreased by 28.0% (95% CI: 22.0–34.0%). Conversely, there were no statistically significant changes in level of WHO level 2 drug utilization rates.

In the year and a half after Medicare Part D was implemented, the trend in use of other WHO level 3 drugs and WHO level 2 drugs approached or surpassed what would have been expected had Medicare Part D not been implemented. For all WHO level 3 drugs, the decreases seen in February 2006 were followed by rates returning to pre-Medicare Part D levels (increases of 1.0% per month). Although monthly rates of fentanyl patch receipt and therapy days covered stabilized, they did not return to the increasing monthly rates seen in 2005. The models demonstrate a -2.0% and a -4.0% change in the post- versus pre-Medicare Part D slopes for rate of fentanyl patch receipt and rate of therapy days covered, respectively. Conversely, utilization rates of other WHO level 3 drugs saw increases that were greater in the post- versus pre-Medicare Part D periods, with both rates of medication receipt and therapy days covered increasing by 2.0% per month. Although Medicare Part D had no measureable effect on the rate of WHO level 2 drug receipt, the rate of therapy days covered increased 1.0% per month.

Sensitivity analyses showed the effects of Medicare Part D on opioid use were substantively unchanged among the dual-eligible beneficiaries (**Table A-4**).

3.4 Discussion

Medicare Part D appeared to have had unintended effects on opioid use among nursing home residents with cancer who experienced pain. Immediately following

implementation of Medicare Part D, there were reductions in the rate of fentanyl patch and other strong opioid use among nursing home residents and the rate of therapy days covered for all opioids. During the 18 months subsequent to Medicare Part D implementation, there were continued decreases in fentanyl patch use. These data support the notion that potential substitutions with other strong opioids and less potent opioids occurred, and suggest that the impact of Medicare Part D extended beyond the explicitly excluded drugs and drug classes.

Our findings are consistent with the only other study (to our knowledge) that focused on use of long-acting opioids among Medicare Part D beneficiaries. During the first year of Medicare Part D, the adjusted risk of ≥30-day gaps in medication use was 0.41 among nursing home residents whose Medicare Part D plans did not cover their long-acting opioids, versus 0.27 among those with more generous plans ($P = 0.0002$).[86] However, gaps in medication use did not appear to result in higher rates of hospitalizations or deaths among nursing home residents. Neither our study nor previous work quantified the impact of these Medicare Part D-induced interruptions on quality of nursing home residents' experiences at the end of life.

Generic versions of the fentanyl patch became available in January 2005 and may explain the steep monthly increases in medication use through 2005. Despite potential increased access to fentanyl patches, we observed interruptions in overall opioid use with the introduction of Medicare Part D. Moreover, these observed patterns occurred even with multiple checks and balances in place in the nursing home setting to protect residents' receipt of high-quality pain management. For example, the Federal Nursing

Home Reform Act (part of the Omnibus Budget Reconciliation Act of 1987), requires that nursing homes provide all medications needed to fulfill residents' care plans.[91] Moreover, CMS began testing pain-focused quality indicators in 1998[70] and required public reporting of the prevalence of uncontrolled pain beginning in 2002.[60] Others have shown that access to alternate formulations of medications used by nursing home residents was affected by limited coverage and frequent use of prior authorization in the first year of Medicare Part D.[93] It is likely that these findings underestimate the impact that Medicare Part D may have had in settings that lack the safeguards present in nursing homes.

The clinical impact of Medicare Part D on long-term trends in fentanyl patch use is unclear. There are concerns about the use of fentanyl patches for initial therapy. Use of fentanyl patches for infrequent or mild pain, or for acute pain following surgery, may lead to respiratory depression and death.[87] Furthermore, increased caution is necessary when using fentanyl patches in treating older adults, whose decreased lean body mass leads to changes in absorption and increased levels of fentanyl.[94] Although our study did not evaluate the effect of Medicare Part D policy on nursing home residents' pain experiences, there is evidence that inadequately treated pain has numerous pathological consequences, including depression, anxiety, sleep disturbance, decreased socialization, and impaired mobility.[20–22] Fentanyl patches may be used during opioid rotation to attenuate the development of tolerance to other long-acting opioids.[68] Its parenteral mode of administration could be important for nursing home residents with feeding tubes or difficulty swallowing tablets. Moreover, use of sustained-release fentanyl patches instead

of shorter-acting oral opioids may simplify otherwise complicated medication regimens, which average 8.8 unique medications among older nursing home residents with cancer.[89] Alleviation of pain is an essential component of high-quality care for people who are nearing the end of life.[95] When used as indicated, fentanyl patches can be part of an effective regimen for treating persistent pain among older adults.

This study has several strengths. This is the first empirical evaluation of Medicare Part D's impact on opioid use among nursing home residents with cancer. An additional strength is our novel use of segmented regression of interrupted time-series data to empirically evaluate the effects of a national policy change on opioid use. This analytic method is one of the strongest quasi-experimental designs to evaluate the effects of time-delimited interventions. Compared to weaker observational study designs, it is robust to many of the threats to internal validity,[55] including time-invariant confounders in the study population and historical changes in fentanyl patch and other opioid use. Furthermore, the nationally representative administrative database did not account for actual enrollment of nursing home residents into Medicare Part D and spanned a variety of payment sources. Therefore, we avoided introduction of selection bias inherent in comparisons of medication use between beneficiaries who did and did not enroll in Medicare Part D.

Several limitations should be noted. The segmented regression methods aggregated individual-level data by time point. As such, our analysis did not adjust for individual-level characteristics. However, pre- and post-Medicare Part D comparisons of the study population confirm that resident characteristics did not appreciably vary

between the two time periods. Evaluating Medicare Part D's impact on longer-term trends in fentanyl patch and other opioid use was beyond the scope of the data. However, we are unaware of similar large-scale drug policies that may have shifted observed opioid use patterns among nursing home residents with cancer in the years since Medicare Part D was first implemented. The pharmacy dispensing records available did not permit us to evaluate the clinical appropriateness of drugs prescribed. Lastly, our analyses included Medicare-eligible nursing home residents with cancer whose prescriptions were filled by a single long-term care pharmacy. Caution should be taken when generalizing the findings to the larger population of nursing home residents with cancer.

3.5 Conclusion

Intended and unintended effects should be carefully measured before—and continually reassessed in the years after—large-scale health policies are implemented. This quasi-experimental study demonstrated that the January 2006 implementation of Medicare Part D led to immediate and continued reductions in receipt of fentanyl patches among nursing home residents with cancer. These medication use patterns occurred despite secular trends that may have otherwise increased access to fentanyl patches and pain management safeguards in the nursing home setting. The clinical impact of these interruptions is uncertain, and it was beyond the scope of this study to quantify the impact of Medicare Part D on quality of life among nursing home residents with cancer. In light of these patients' residence in a medically supervised setting and consequent low potential for medication abuse, expansion of Medicare Part D's coverage of pain

medication and alternative opioid formulations should be considered for this vulnerable population.

Figure 3-1. Sample Selection Strategy

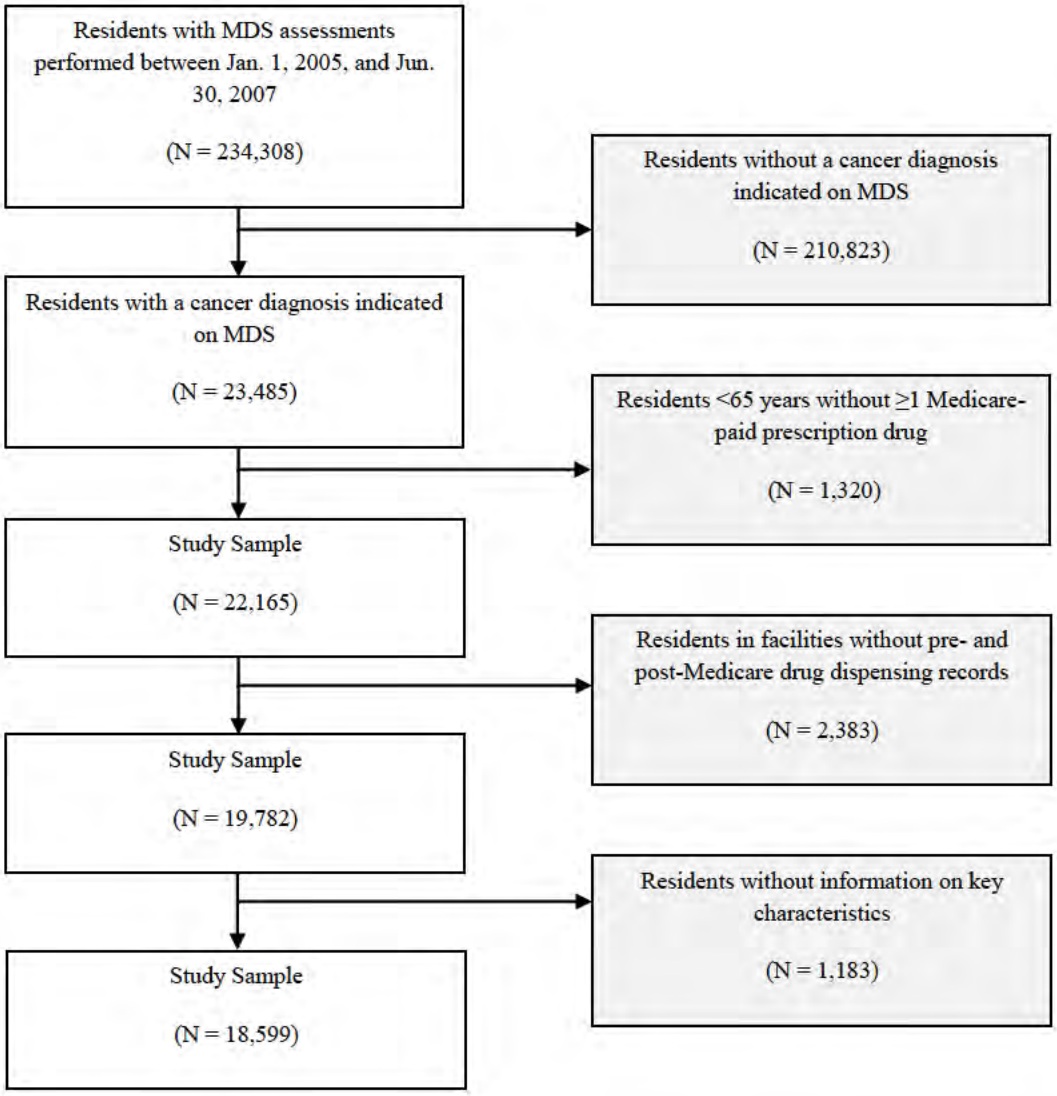


Table 3-1: Characteristics of Nursing Home Residents with Cancer, Pre- and Post-Medicare Part D Implementation

	Pre-Medicare Part D (Jan 2005–Dec 2005) n = 10,392	Post-Medicare Part D (Feb 2006–Jun 2007) n = 12,999
Age		
<65	4.2	5.2
65–74	17.7	17.9
75–84	41.9	40.2
≥85	36.2	36.7
Women	57.0	56.4
Race and ethnicity		
Non-Hispanic white	84.6	83.3
Non-Hispanic black	10.7	11.2
Hispanic	3.3	3.8
Asian or Pacific Islander	1.2	1.6
American Indian or Alaskan Native	0.2	0.2
Widowed	49.4	47.7
Source of admission[b]		
Acute care hospital	80.3	81.6
Private home	8.1	7.8
Other nursing home	6.5	5.9
Other[c]	5.0	4.8
US census region		
South	30.8	31.3
West	14.6	17.2
Midwest	35.3	32.7
Northeast	19.3	18.8
Degree of functional impairment[d]		
Moderate	44.7	47.5
Severe	27.0	24.6
Degree of cognitive impairment[e]		
Moderate	48.9	46.8
Severe	8.3	6.8
Depressed mood[f]	10.9	10.1
Bedfast	4.8	3.8
Terminal prognosis[g]	9.7	7.8
Number of diagnoses	6.6 ± 2.7 (1–20)	6.4 ± 2.6 (1–19)
Clinical conditions		
Arthritis	29.0	26.7
Osteoporosis	15.9	14.6
Hip fracture	5.7	6.1
Number of unique medications	3.4 ± 2.4 (1–12)	3.9 ± 3.0 (1–16)
Pain[h]	55.9	58.4

	Pre-Medicare Part D (Jan 2005–Dec 2005) n = 10,392	Post-Medicare Part D (Feb 2006–Jun 2007) n = 12,999
Daily	23.4	24.2
Less than daily	32.5	34.1

$N_{residents}$ = 18,599 (4,792 nursing home residents were observed in both periods)
$N_{facilities}$ = 1,112
Percentage and mean ± standard deviation (range) shown.
[a] 5,093 missing information on source of admission.
[b] Includes board and care/assisted living/group home, psychiatric hospital, rehabilitation hospital.
[c] Based on a 7-level scale: Activities of Daily Living Hierarchy Scale score of 3 or 4 for moderate impairment, 5 or 6 for severe impairment.[41]
[d] Based on a 7-level scale: Cognitive Performance Scale scores of 2 to 4 for moderate impairment, 5 or 6 for severe impairment.[43]
[e] Based on a scale from 0–14: Depression Rating Scale scores ≥3 indicate major or minor depressive disorders.[42]
[f] Indicated by prognosis of <6 months or receipt of hospice.
[g] As assessed by nursing home staff over a 7-day period.

Figure 3-2. Impact of Medicare Part D on Rate of Opioid Receipt and Rate of Therapy Days Covered in Nursing Home Residents with Cancer, Jan 2005–Jun 2007

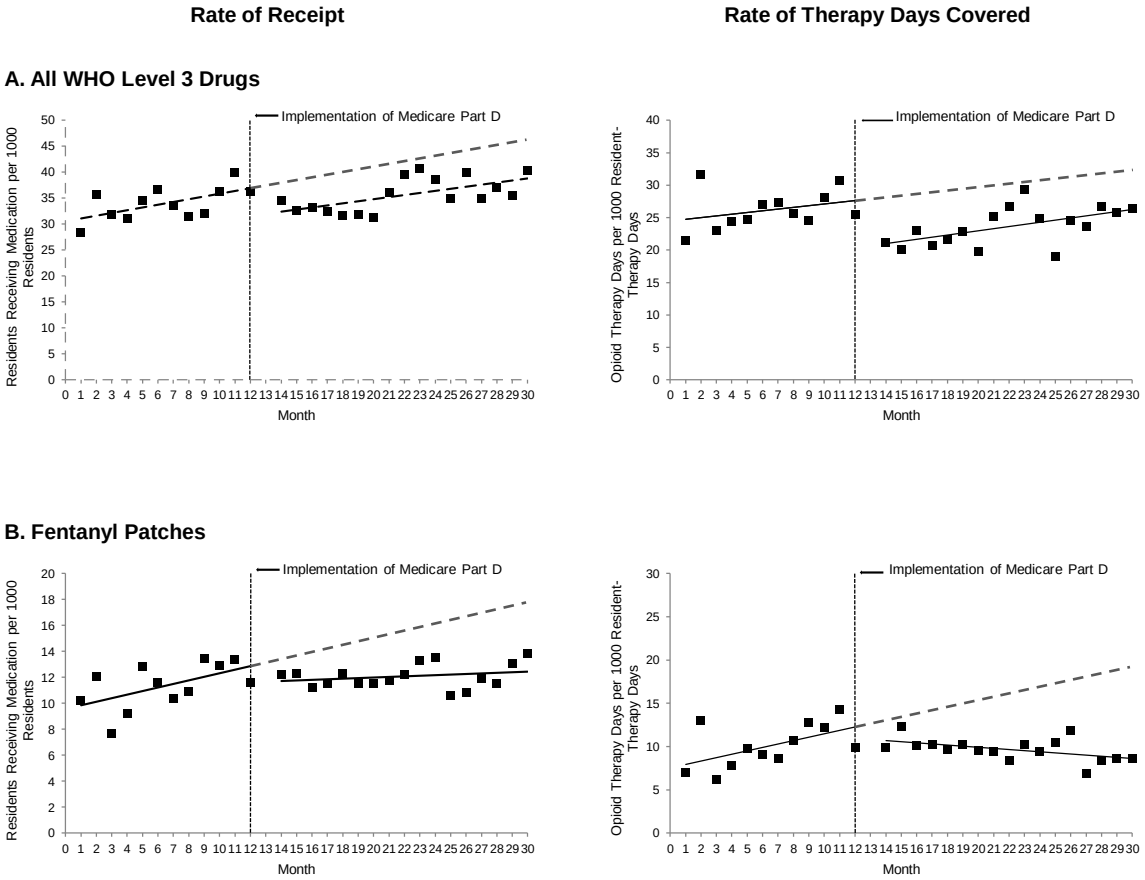
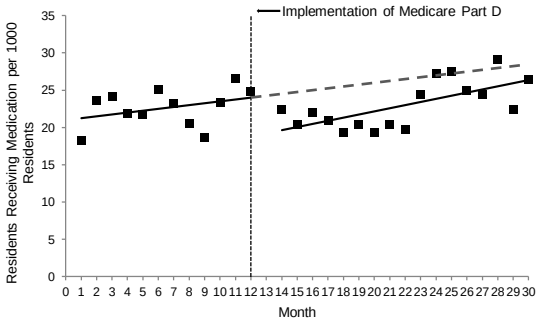
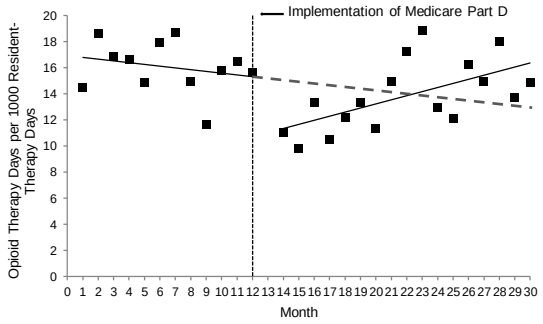


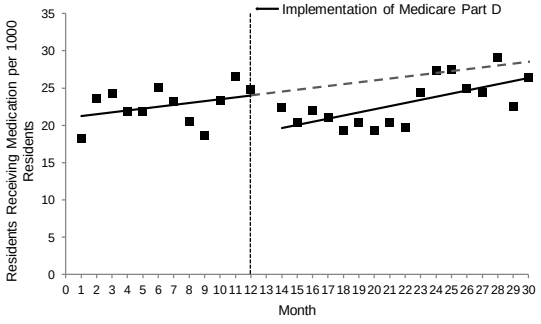
Figure 3-2, Continued. Impact of Medicare Part D on Rate of Opioid Receipt and Rate of Therapy Days Covered in Nursing Home Residents with Cancer, Jan 2005–Jun 2007

C. Other WHO Level 3 Drugs (Excluding Fentanyl Patches)





D. All WHO Level 2 Drugs



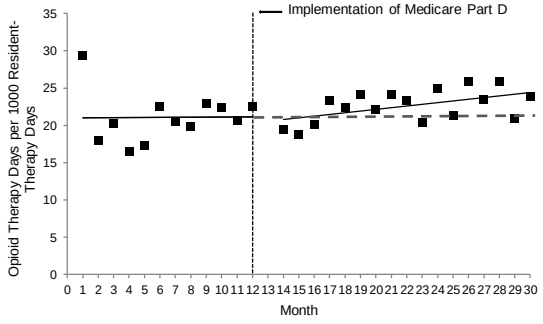


Table 3-2: Impact of Medicare Part D on A) Rate of Opioid Receipt and B) Rate of Opioid Therapy Days Covered in Nursing Home Residents with Cancer, Jan 2005–Jun 2007

A. Rate of opioid receipt

	WHO level 3 drugs						WHO level 2 drugs	
	All		Fentanyl patch		Other WHO level 3 drugs			
	IRR[a]	95% CI	IRR[a]	95% CI	IRR[a]	95% CI	IRR[a]	95% CI
Pre-Part D Slope	1.02	1.01–1.02	1.02	1.02–1.03	1.01	1.01–1.02	1.01	1.00–1.02
Post-Part D Slope	1.01	1.01–1.01	1.00	1.00–1.01	1.02	1.01–1.02	1.01	1.00–1.01
Change in rate in February 2006	0.87	0.83–0.89	0.90	0.87–0.93	0.79	0.75–0.84	1.02	0.95–1.09
Change in slope (after vs before Part D)	1.00	0.99–1.00	0.98	0.97–0.99	1.01	1.00–1.01	0.99	0.99–1.00

B. Rate of opioid therapy days covered

	WHO level 3 drugs						WHO level 2 drugs	
	All		Fentanyl patch		Other WHO level 3 drugs			
	IRR[a]	95% CI	IRR[a]	95% CI	IRR[a]	95% CI	IRR[a]	95% CI
Pre-Part D Slope	1.01	1.01–1.01	1.04	1.03–1.05	0.99	0.99–1.00	1.00	0.99–1.01
Post-Part D Slope	1.01	1.01–1.02	1.00	0.99–1.01	1.02	1.02–1.03	1.01	1.01–1.01
Change in rate in February 2006	0.74	0.72–0.77	0.78	0.72–0.84	0.72	0.66–0.78	0.97	0.90–1.04

	WHO level 3 drugs						WHO level 2 drugs	
	All		Fentanyl patch		Other WHO level 3 drugs			
	IRR[a]	95% CI	IRR[a]	95% CI	IRR[a]	95% CI	IRR[a]	95% CI
Change in slope (after vs before Part D)	1.00	1.00–1.01	0.96	0.95–0.97	1.03	1.02–1.04	1.01	1.00–1.02

CI: confidence interval; **IRR:** incidence rate ratio

[a] Adjusted for serial correlation using Newey-West standard errors

CHAPTER IV:

NAÏVE INITIATION OF LONG-ACTING OPIOIDS IN NURSING HOME RESIDENTS

ABSTRACT

BACKGROUND: Despite known risks of overdose and respiratory depression when treating opioid-naïve individuals with long-acting opioids, use of these potent agents may be common in nursing homes. Our objective was to estimate the prevalence of naïve initiation of long-acting opioids since national efforts to increase prescriber and public awareness on the safe use of these potent medications.

METHODS: This cross-sectional study included 9,543 Medicare-enrolled, long-stay nursing home residents in 3,018 US nursing homes. The MDS 3.0 linked with Medicare enrollment, hospital claims, and prescription drug transaction data (January-December 2011) were used to determine the prevalence of naïve initiation among nursing home residents who initiated a long-acting opioid in the nursing home. Binomial logistic regression was used to evaluate resident-level correlates of naïve-initiation of a long-acting opioid.

RESULTS: Of nursing home residents who initiated a long-acting opioid within 30 days of a nursing home admission, 10.0% (95% CI: 9.4–10.6%) had not used an opioid in the previous 60 days. Naïve initiation of long-acting opioids was positively associated with life expectancy <6 months (adjusted OR = 1.96, 95% CI: 1.58–2.43), moderate/severe functional impairment (adjusted OR = 1.32, 95% CI: 1.12–1.55), feeding tubes (adjusted OR = 1.53, 95% CI: 1.15–2.04), and a cancer diagnosis (adjusted OR = 1.39, 95% CI: 1.16–1.67).

CONCLUSION: Naïve initiation of long-acting opioids persists in nursing homes, especially among residents who may require alternative opioid formulations or who are at the end of life.

4.1 Introduction

Opioid analgesics are essential treatment options for people who suffer from moderate to severe pain. In nursing homes—medically supervised settings that have frequent use of medications for end-of-life care[31]—use of these potent agents is common. In **Chapter II**, we reported that among nursing home residents with a diagnosis of cancer, an estimated 36% of those with daily severe pain, and 21% of persons with daily moderate pain, received a long-acting opioid during the first week of a nursing home stay.[89] Despite their useful role in pain management, risks of opioid use in nursing home residents should not be minimized. In the nursing home setting, opioids were among the top five drugs associated with overall adverse drug events and preventable adverse drug events.[96]

The FDA requires that "boxed" warnings appear on the labels or package inserts of long-acting opioids to call attention to their use in opioid-tolerant patients only. Long-acting opioids are potent drugs with prolonged time to elimination. Improper use of long-acting opioids is associated with substantial health risks, such as fatal overdose because of respiratory depression among patients not already tolerant to high doses of opioids. In July 2005 and December 2007, the FDA issued public health advisory warnings to alert health care providers, patients, and caregivers on the safe use of transdermal fentanyl systems (patches).[87,97] The only study (to our knowledge) to estimate the prevalence of naïve initiation of long-acting opioids in the nursing home setting used Rhode Island Medicaid data from 2004 and 2005.[32] In this study, 39.3% of nursing home residents who received a long-acting opioid had not used any opioid in the previous 60 days.[32] Whether

the prevalence of naïve initiation of long-acting opioid use in nursing homes has declined since the FDA advisories is unknown.

An update to our current understanding of the prescribing of long-acting opioids to opioid-naïve nursing home residents is needed. FDA safety communications have reduced the use of antipsychotics in older adults with dementia,[98] long-acting β-agonists in patients with asthma,[99] antidepressants in young adults with new-onset depression,[100] and rosiglitazone for the treatment of type 2 diabetes.[101–103] We hypothesized that the prevalence of naïve initiation would have declined in light of efforts to increase prescriber and public awareness on the safe use of long-acting opioids. Therefore, we used recent national data of Medicare beneficiaries to estimate the prevalence, and to identify correlates, of naïve-initiation of long-acting opioids in nursing homes.

4.2 Methods

The institutional review board of the University of Massachusetts Medical School approved this study.

4.2.1 Data Sources

We used four data sources: 1) MDS version 3.0, 2) Master Beneficiary Summary Files that determine Medicare enrollment, 3) MedPar files containing hospital claims data, and 4) Medicare Part D prescription drug transaction data.

MDS 3.0 is a systematic and comprehensive assessment of care planning and resident health that consists of sociodemographic information; clinical items (e.g., falls and balance items, bladder and bowel, communication, behavior, signs, symptoms);

active diagnoses; and treatments, procedures, and programs.[44,45] Nursing home providers are required to perform full assessments on residents at the time of nursing home admission and annually thereafter ;a subset of the MDS items are assessed quarterly or when a resident experiences a significant change in health status.[44]

MDS 3.0 is a revision of MDS 2.0 (used from 1999 to 2010) and was implemented in all Medicare- and Medicaid-certified nursing homes in October 2010. It is widely accepted for research purposes and, compared with earlier versions of the resident assessment instrument, offers improved quality and completeness of some data constructs, including symptoms and psycho-social experiences.[104] The most significant conceptual departure from MDS 2.0 is the inclusion of direct resident interviews to assess key domains of health. Although resident interviews are the preferred method for completing the assessment, nursing home staff may answer alternative observation items on behalf of residents who cannot make themselves understood at least some of the time or who cannot complete an interview. Family members or significant others may answer items regarding resident preferences.

4.2.2 Study Sample

As shown in **Figure 4-1**, the sample frame for this study was 3,273,636 Medicare-enrolled nursing home residents with an admission assessment performed between January 1, 2011, and December 31, 2011. We required that residents have a nursing home stay ≥90 days (n = 1,103,195), as Medicare Part D prescription drug transaction data may not include medications associated with skilled nursing facility care covered by Medicare

Part A. We excluded residents who were admitted to the nursing home between January 1, 2011, and March 31, 2011 (n = 130,598) because we were unable to observe ≥90 days of their medication use prior to nursing home admission. We also excluded residents who were comatose (n = 3,479); who did not initiate a long-acting opioid after nursing home admission (n = 949,965); who did not have three months of continuous enrollment in Medicare Part D prior to initiation of a long-acting opioid in the nursing home (n = 1,176); who had a hospital admission in the seven days prior to initiation of a long-acting opioid in the nursing home (n = 874); or who were missing information on key sociodemographic or clinical characteristics (n = 1,041). We identified a total of 16,062 nursing home residents who met these eligibility criteria. Although we estimated the proportion of residents naively initiating a long-acting opioid using several subsamples derived from this sample, the primary analysis was conducted in 9,543 residents admitted to 3,018 facilities who initiated a long-acting opioid in the first 30 days of nursing home admission.

4.2.3 Measurement of Opioid Use and Opioid Tolerance

We used Medicare Part D prescription drug transactions from January 1, 2011, to December 31, 2011. Data elements included brand and generic names of all prescription drugs dispensed to nursing home residents, product identification code (NDC), service date, days' supply, quantity dispensed, drug strength, and drug formulation.
The Multum® drug database was used to code drug names and to map those names to therapeutic categories.

The primary outcome of interest was naïve initiation of a long-acting opioid within the first 30 days of a nursing home admission. We categorized opioid analgesics by duration of effect (i.e., long-acting, short-acting) according to recent clinical practice guidelines that consider pain management by level of opioid-tolerance.[10,50,51] Long-acting opioids included controlled- or extended-release formulations of hydromorphone, morphine sulfate, oxycodone, oxymorphone, and tramadol, as well as any dose of a fentanyl or buprenorphine patch. Short-acting opioids included immediate-release formulations of buprenorphine, butorphanol, codeine, fentanyl, hydrocodone, hydromorphone, meperidine, morphine sulfate, nalbuphine, opium, oxymorphone, oxycodone, pentazocine, tapentadol, and tramadol. Opioids combined with acetaminophen or non-steroidal anti-inflammatory drugs, which limit the maximum daily dose because of risks of liver and gastrointestinal toxicity, were also considered as short-acting agents.[52] CMS quality indicators include the prevalence of uncontrolled moderate-to-severe pain occurring within the first 14 days of nursing home admission.[105] We evaluated the first 30 days of a nursing home stay based on the expectation that initial provision of analgesic medications would occur shortly after admission.

To facilitate comparison with published estimates of naïve-initiation of long-acting opioids in nursing home residents,[32] individuals were considered opioid-naïve if they had not used a short- or a long-acting opioid in the 60 days preceding initial receipt of a long-acting opioid after a nursing home admission. Since some states limit prescriptions of controlled substances to a 30-day supply,[106] we expected a 60-day look back period to capture intermittent use of opioid analgesics. We also evaluated initiation

of long-acting opioids within different time periods after nursing home admission (7 days [n = 5,298]; 14 days [n = 6,507]; 60 days [n = 12,381]; 90 days [n = 13,782]; and anytime [n = 16,062]).

4.2.4 Measurement of Correlates

Correlates were selected based on previous evidence of association with naïve initiation of long-acting opioids[32] and were drawn from MDS admission assessments. Key sociodemographic characteristics included age, sex, and race/ethnicity. Clinical characteristics included source of nursing home admission (acute hospital, community, other); life expectancy of <6 months at nursing home admission; need for parenteral feeding or feeding tube; difficulty chewing; difficulty swallowing; resident rejection of care "necessary to achieve the resident's goals for health and well-being";[44] active diagnoses that may impact analgesic treatment; functional status; cognitive status; and pain. Functional status was based on the Resource Utilization Groups-III ADL scale, with scores ranging from 4 (no impairment) to 18 (severe impairment).[46] Cognitive status was based on the Cognitive Function Scale, with residents categorized as cognitively intact, mildly impaired, moderately impaired, or severely impaired.[47] Section J of the MDS 3.0 defined pain as "pain or hurting at any time" during the five days preceding the assessment.[44] One item addressed pain frequency (rarely/occasionally, frequently/almost constantly). Per guidance by Edelen and Saliba,[63] we combined responses from the numeric rating and verbal descriptor scales to characterize pain intensity (mild, moderate, severe/very severe).[63]

4.2.5 Statistical Analysis

First, we estimated the proportion of residents with naïve initiation of long-acting opioids by varying the look back period (30 days, 60 days, or 90 days) and the time since nursing home admission (7 days, 14 days, 30 days, 60 days, 90 days, or anytime). We performed these sensitivity analyses to facilitate comparisons with previous work.[32] Second, using the sample for the primary outcome of interest (i.e., naïve initiation within the first 30 days of nursing home admission, with a 60 day look back period), we described resident-level characteristics by source of nursing home admission (i.e., acute setting, community, other). With the sample size available, trivial differences in the distributions achieved statistical significance. As such, absolute differences in percentages of >5% were considered noteworthy.

We developed a binary logistic model to estimate associations among resident-level correlates and naïve initiation of long-acting opioids. Before constructing the model, we calculated correlations among variables. No variable pairs were highly collinear (>0.90); therefore, we included all correlates of interest in the model. The logistic model was fit using robust estimation of standard errors to account for correlation between residents within the same nursing home.[69] Unadjusted and adjusted ORs and 95% CIs were derived from the models.

In a sensitivity analysis, we separately evaluated residents with a cancer diagnosis (n = 1,660), as long-acting opioids are accepted treatment options for cancer-related pain.[10,50,51] Cancer was indicated in MDS Section I "Active Diagnoses" through a check box or ICD-9-CM codes 140.XX–203.XX. We also performed sensitivity analyses where

we: 1) evaluated initiation of a long-acting opioid anytime after a nursing home admission and 2) varied the definition of opioid-naiveté to non-receipt of an opioid in the previous 90 days before long-acting opioid initiation. All analyses were performed using Stata version 11.2 (StataCorp LP, College Station, TX).

4.3 Results

Figure 4-2 shows estimates of naïve long-acting opioid initiation using different look back periods and at different times since nursing home admission. Of all residents who received a long-acting opioid in the nursing home, nearly 30.0% initiated within the first week of admission and 59.4% within the first 30 days. The proportion with naïve initiation of long-acting opioids was 13.9–27.5% using a 30-day look back period, 9.7–18.6% using a 60-day look back period, and 6.6–11.8% using a 90-day window. Regardless of look back period, estimates of naïve initiation were similar within 30 days of admission (e.g., 9.7% in those initiating a long-acting opioid in the first 7 days and 10.0% in the first 30 days of admission). Of residents who initiated a long-acting opioid within 30 days of admission, 10.0% (95% CI: 9.4–10.6%) had not used an opioid analgesic in the previous 60 days.

The majority (58.3%) of residents were admitted to the nursing home from an acute hospital (**Table 4-1**). Residents had a mean age of 75.0 ± 13.3 years, 72.2% were female, and 86.4% were non-Hispanic white. Nearly 71.2% of residents had moderate to severe functional impairment and 21.6% had moderate to severe cognitive impairment. Overall, 86.9% had pain documented, among whom 31.5% had moderate or severe pain

and 73.4% had frequent or almost constant pain. Compared to their counterparts admitted from the community or other non-acute setting, those admitted from an acute hospital were younger and more likely to have hip fracture, stroke, and documented pain. However, they were less likely to have cognitive impairment, Alzheimer disease, arthritis, osteoporosis, and a terminal prognosis. Among residents with documented pain (86.9%), those admitted from an acute care setting were more likely than residents from a non-acute setting to have experienced pain constantly during the five days prior to assessment; however, that pain was more likely to be mild.

Women and nursing home residents with arthritis or stroke had decreased odds of naively initiating a long-acting opioid (**Table 4-2**). Compared with residents admitted to the nursing home from a community setting, residents from another non-acute setting or an acute hospital were more likely to have naively initiated a long-acting opioid. Similarly, nursing home residents with a terminal prognosis, functional impairment, feeding tubes, and cancer were more likely to have naively initiated a long-acting opioid.

Among nursing home residents with cancer (n = 1,660), naïve long-acting opioid initiation was positively associated with terminal prognosis, functional impairment, and hip fracture (**Table A-5**). The sensitivity analyses in which we evaluated long-acting opioid initiation anytime after nursing home admission (**Table A-6**) and extended the look back period to 90 days (**Table A-7**) were generally consistent with results found in the primary analysis. However, the former analysis found an increased likelihood of naïve initiation in residents with pulmonary conditions and decreased likelihood in

residents with osteoporosis. In the latter analysis, we did not find statistically significant associations of naïve initiation among women or residents with a feeding tube or stroke.

4.4 Discussion

This study demonstrates that 10% of nursing home residents who received a long-acting opioid in the first month of nursing home admission had not previously been on opioid therapy. These results are significantly decreased from those documented before large-scale changes to analgesic medication use in the nursing home setting. Residents with functional impairments, feeding tubes, cancer, or terminal prognosis at nursing home admission had increased odds of naively initiating a long-acting opioid.

Dosa and colleagues estimated that approximately 39.3% of nursing home residents who received a long-acting opioid in the nursing home had not previously been on opioid therapy.[32] However, our estimates of naïve initiation using varied definitions of opioid naivety fell below this estimate (**Figure 4-2**); indeed, when we used similar parameters (i.e., 60-day look back and initiation of a long-acting opioid anytime after nursing home admission), 18.6% of nursing home residents who received a long-acting opioid were opioid-naïve. Our results may differ from earlier estimates because of the previous study's small sample size, focus on nursing homes residents in one state (Rhode Island), and use of data that predated national changes to medication use in the nursing home setting and campaigns to increase awareness around safe opioid analgesic use.

We anticipated changes in the provision of long-acting opioids since the mid-2000s for several reasons. In March 2009, CMS revised surveyors' interpretative

guidelines for meeting compliance in the evaluation and management of pain in nursing home residents (F-Tag 309). Lapane and colleagues showed that these revisions improved nursing home providers' recognition and management of pain, and also increased use of opioid analgesics among nursing home residents with documented non-cancer pain.[107] Moreover, we demonstrated in **Chapter III** that the January 2006 implementation of the Medicare Part D prescription drug benefit may have impacted use of opioids in the nursing home setting. Specifically, Medicare Part D led to sustained reductions in the use of fentanyl patches and potential substitution of these long-acting opioids with other strong opioids and less potent opioids to treat residents with cancer.

Both the FDA and clinical guidelines for pain management in older adults strongly advise against the use of long-acting opioids to treat patients who are not already tolerant to high doses of opioid therapy.[87,68,97] Serious adverse effects associated with improper use of long-acting opioids include respiratory depression and unintentional overdose. However, there are some individuals whose clinical needs require adjustments to the recommended course of stepped therapy. We found evidence of increased naïve initiation of long-acting opioids among nursing home residents with functional impairment and feeding tubes, who may be unable to tolerate oral formulations or frequent dosing of short-acting analgesics. Residents with cancer and terminal prognosis were also more likely to have naively initiated a long-acting opioid. The need to effectively control moderate-to-severe pain and provide patient comfort at the end of life may outweigh the risk of potential adverse drug effects. This is consistent with studies

that have found increased polypharmacy–especially with medication for symptom control[108,109]–after referral to palliative care.[108–111]

The landscape of opioid prescribing in long-term care continues to change. In July 2012, the FDA approved a class-wide Risk Evaluation and Mitigation Strategy (REMS) for long-acting opioids. The purpose of the REMS is to, "reduce serious adverse outcomes resulting from inappropriate prescribing, misuse, and abuse of extended-release or long-acting opioid analgesics while maintaining access to pain medications."[112] Through the REMS, the FDA requires pharmaceutical companies and distributors to provide education for medication prescribers and resources for counseling patients about the risks and benefits of long-acting opioid use. Failure to comply with these strategies may result in financial penalties of up to $10 million, and a long-acting opioid may be deemed to be misbranded.[113] Future research is needed to evaluate the extent to which these dramatic changes in medication safety strategies actually reach health care providers in nursing homes and, consequently, impact the quality of opioid therapy in this setting.

The present study has several strengths worth highlighting. First, we used national data from CMS to provide new evidence on long-acting opioid use in a large, national sample of Medicare beneficiaries residing in nursing homes. Second, we used nursing home residents assessments from the MDS 3.0, which emphasizes direct resident interviews and thus offers improved quality and completeness of information on symptoms and other subjective constructs.[104] Third, our use of Medicare Part D prescription drug transactions allowed for evaluations of opioid use before and after

nursing home admission. Finally, we included in our study sample nursing home residents who received any extended- or controlled-release opioid analgesic. Previous work evaluated only those who initiated a fentanyl patch, long-acting oxycodone, or long-acting morphine sulfate.

There were also some limitations. Due to our reliance on prescription drug transactions from a single payer, there is potential misclassification of nursing home residents as opioid-naïve. For example, we expected that residents admitted from an acute hospital would be less likely than their community-based counterparts to experience naïve long-acting opioid initiation, yet we demonstrated the opposite relationship. The lack of all-payer drug dispensing records may, therefore, have resulted in an overestimation of the proportion of nursing home residents who naively initiated a long-acting opioid. Moreover, our definition of naïve-tolerance is very liberal; we considered a nursing home resident to be opioid-tolerant if they used *any* dose of opioid analgesic prior to initiating a long-acting opioid.

4.5 Conclusion

This study provides a timely update to what is known about potentially inappropriate use of long-acting opioids in nursing home residents. Recent efforts to improve the quality of medication use and to increase awareness around the safe use of opioid analgesics may have had a positive effect on pain management in nursing homes. However, special attention should continue to be paid to nursing home residents who require alternative opioid formulations or who are at the end of life. Educational efforts

that target medication prescribers should also consider the important roles that non-prescribers (e.g., direct-care nursing staff) play in the provision of high-quality pain management for nursing home residents.

Figure 4-1. Sample Selection Strategy

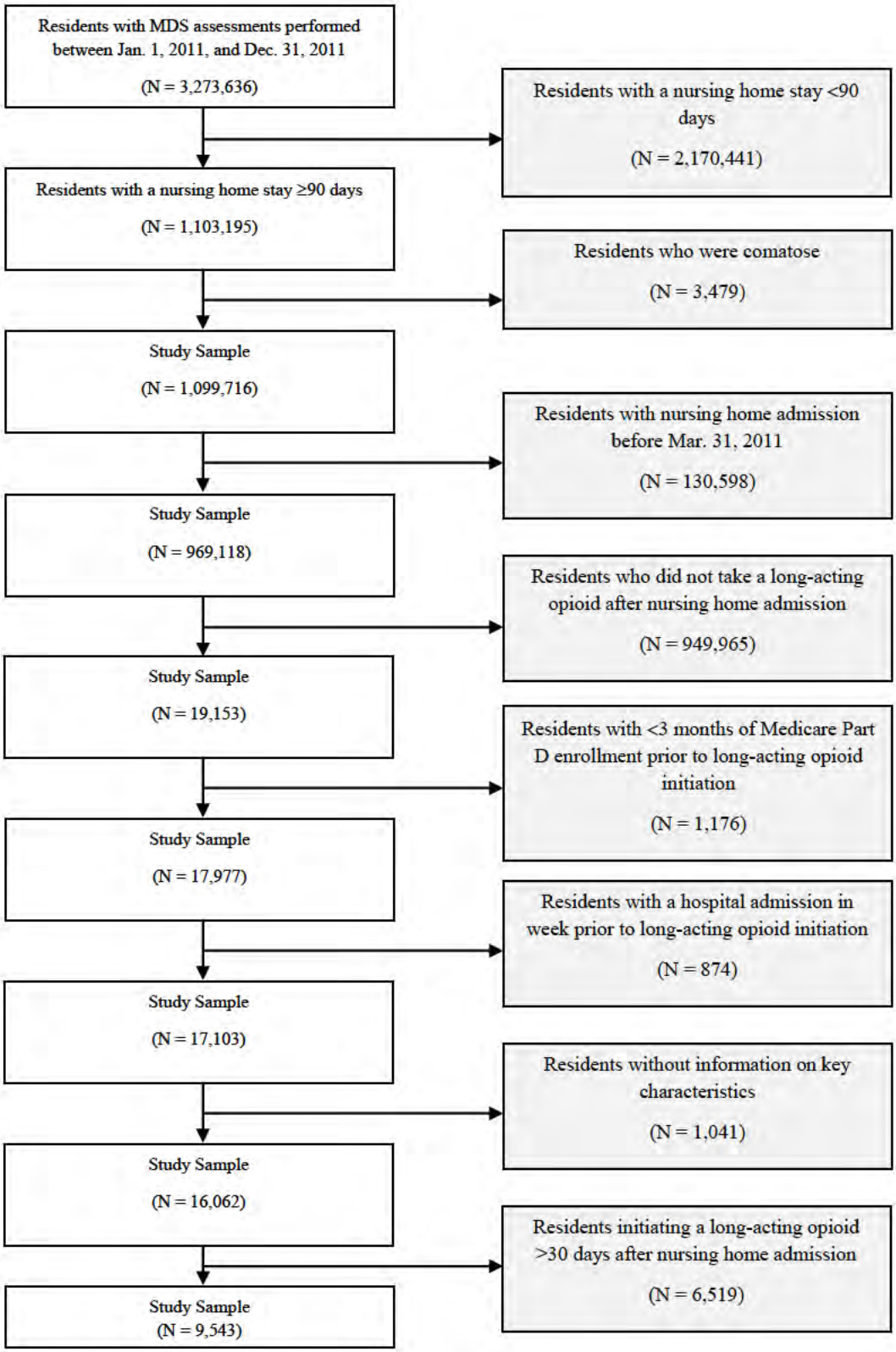


Figure 4-2: Proportion of Nursing Home Residents who Naively Initiated a Long-Acting Opioid, by Time Since Admission and Look Back Period

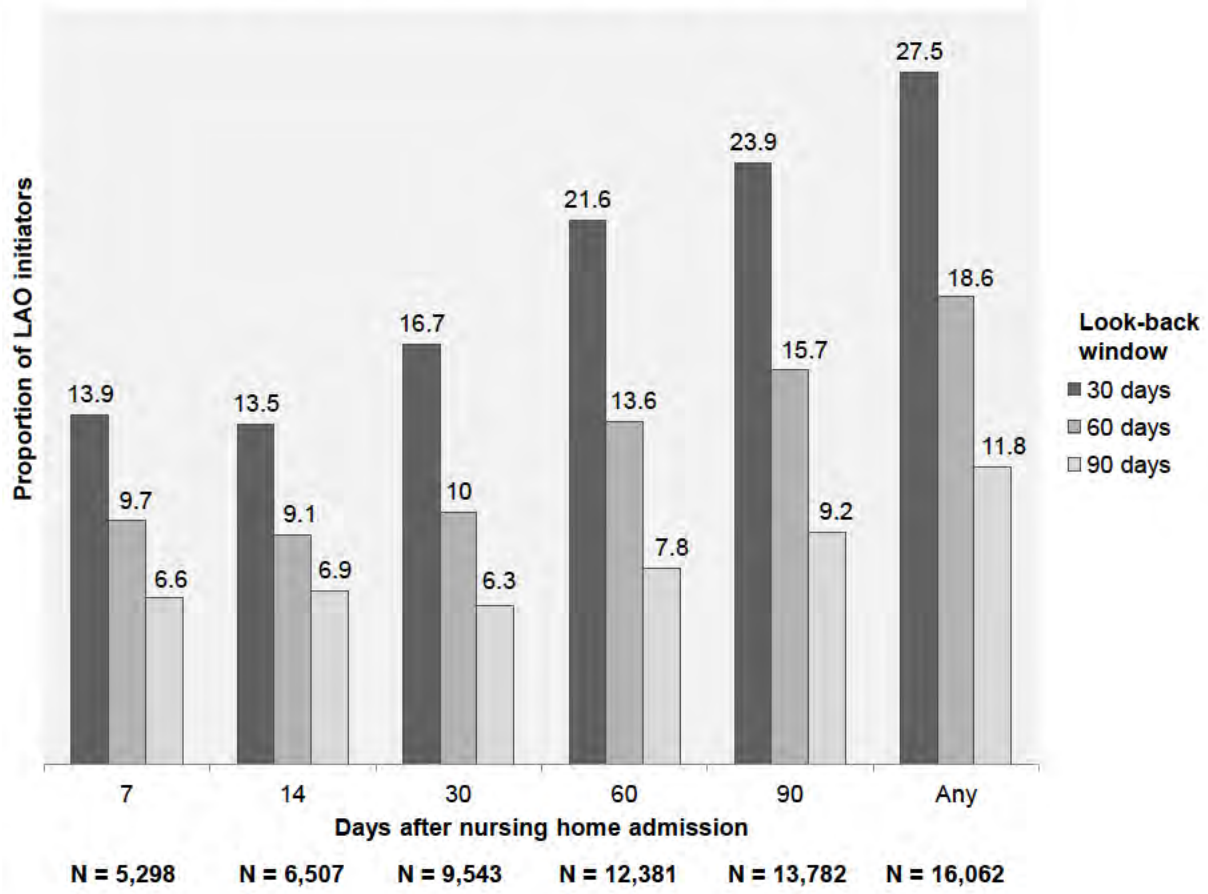


Table 4-1: Characteristics of Nursing Home Residents who Initiated a Long-Acting Opioid, by Source of Admission

	Acute hospital (n = 5,563)	Community[a] (n = 2,252)	Other[b] (n = 1,728)
Age, years			
<65	22.8	13.5	19.7
65–74	26.5	16.3	22.1
75–84	29.3	30.8	29.6
≥85	21.4	39.4	28.7
Women	71.5	76.1	69.7
Race and ethnicity			
Non-Hispanic white	83.1	92.7	89.0
Non-Hispanic black	10.0	4.3	6.9
Hispanic	4.9	1.9	2.9
Asian	1.2	0.4	0.7
American Indian or Alaskan Native	0.4	0.5	0.4
Native Hawaiian or Other Pacific Islander	0.2	0.3	0.1
Multiracial	0.1	0.0	0.2
Life expectancy of <6 months	6.7	11.2	8.9
Degree of functional impairment[c]			
Moderate	47.1	37.4	36.6
Severe	29.0	22.3	33.7
Degree of cognitive impairment[d]			
Moderate	8.9	15.3	17.3
Severe	9.1	8.6	12.7
Parenteral feeding or feeding tube	5.4	1.5	4.1
Difficulty chewing	2.0	2.2	2.7
Difficulty swallowing	5.0	4.7	5.8
Clinical conditions			
Cancer	17.8	19.1	14.0

	Acute hospital (n = 5,563)	Community[a] (n = 2,252)	Other[b] (n = 1,728)
Arthritis	34.2	43.3	38.7
Osteoporosis	17.2	23.0	19.9
Hip fracture	5.6	0.8	2.9
Asthma, chronic obstructive pulmonary disease, or chronic lung disease	29.8	27.0	31.8
Respiratory failure	2.8	0.5	1.2
Heart failure	17.3	19.1	22.3
Alzheimer disease	2.6	7.1	8.0
Stroke	7.6	9.2	13.3
Rejected care	8.4	10.7	13.3
Pain at admission[e]	90.3	83.4	80.5
Pain frequency, if pain present[f]			
Rarely/occasionally	24.9	27.5	31.1
Frequently/almost constantly	75.1	72.5	68.9
Pain severity, if pain present[f]			
Mild	70.7	64.1	67.7
Moderate	15.5	19.9	18.7
Severe/very severe	13.9	16.0	13.6

N = 9,543

Percentages presented.

[a] Includes private home/apartment, board/care, assisted living, and group home.

[b] Includes other nursing home, psychiatric hospital, inpatient rehabilitation facility, mental retardation/developmental disabilities facility, hospice, and other.

[c] Based on scores from 4 to 18: Resource Utilization Groups-III Activities of Daily Living score of 14 to 16 for moderate impairment, 17 or 18 for severe impairment.[46]

[d] Based on 4-level Cognitive Function Scale.[47]

[e] As assessed by resident interview or nursing home staff observation over a 5-day period.

[f] Residents were missing information on pain frequency (n = 92) and pain severity (n = 200).

Table 4-2: Correlates of Naive Long-Acting Opioid Initiation in Newly Admitted Nursing Home Residents

	Naïve initiation (n = 951)	Non-naïve initiation (n = 8,592)	Likelihood of naïve initiation	
			Unadjusted OR (95% CI)	Adjusted[a] OR (95% CI)
Source of admission				
Acute hospital	63.8	57.7	1.66 (1.37–2.00)	1.53 (1.26–1.85)
Community[b]	16.3	24.4	Referent	Referent
Other[c]	19.9	17.9	1.66 (1.32–2.09)	1.62 (1.28–2.04)
Age, years				
<65	21.6	19.9	1.00 (0.82–1.22)	1.04 (0.85–1.28)
65–74	25.0	23.1	Referent	Referent
75–84	31.2	29.5	0.98 (0.81–1.17)	1.08 (0.90–1.31)
≥85	22.2	27.5	0.75 (0.62–0.90)	0.90 (0.74–1.12)
Women	65.6	73.0	0.71 (0.61–0.81)	0.80 (0.69–0.93)
Race and ethnicity				
Non-Hispanic white	84.1	86.7	Referent	Referent
Non-Hispanic black	10.1	7.8	1.33 (1.06–1.66)	1.12 (0.89–1.42)
Hispanic	3.5	3.9	0.92 (0.63–1.34)	0.81(0.55–1.20)
Other[d]	2.3	1.6	1.49 (0.96–2.32)	1.30 (0.81–2.09)
Life expectancy of <6 months	15.9	7.3	2.39 (1.99–2.87)	1.96 (1.58–2.43)
Moderate/severe functional impairment[e]	76.7	70.5	1.37 (1.18–1.60)	1.32 (1.12–1.55)
Moderate/severe cognitive impairment[f]	24.9	21.2	1.23 (1.06–1.44)	1.13 (0.95–1.36)
Parenteral feeding or feeding tube	7.3	3.9	1.92 (1.48–2.50)	1.53 (1.15–2.04)
Difficulty chewing	2.1	2.2	0.96 (0.60–1.53)	0.90 (0.56–1.43)
Difficulty swallowing	5.6	5.0	1.12 (0.84–1.49)	0.92 (0.67–1.25)
Clinical conditions				
Cancer	25.7	16.5	1.75 (1.49–2.05)	1.39 (1.16–1.67)
Arthritis	29.9	37.9	0.70 (0.60–0.80)	0.82 (0.70–0.95)
Osteoporosis	14.6	19.5	0.71 (0.59–0.85)	0.88 (0.72–1.06)

	Naïve initiation (n = 951)	Non-naïve initiation (n = 8,592)	Likelihood of naïve initiation	
			Unadjusted OR (95% CI)	Adjusted[a] OR (95% CI)
Hip fracture	4.7	3.9	1.23 (0.90–1.68)	1.16 (0.84–1.61)
Asthma, chronic obstructive pulmonary disease, or chronic lung disease	32.9	29.1	1.19 (1.03–1.38)	1.16 (1.00–1.35)
Respiratory failure	3.2	1.9	1.72 (1.15–2.56)	1.25 (0.82–1.90)
Heart failure	19.9	18.5	1.09 (0.92–1.30)	1.12 (0.94–1.33)
Alzheimer disease	3.8	4.7	0.80 (0.57–1.12)	0.95 (0.66–1.36)
Stroke	7.5	9.2	0.80 (0.62–1.02)	0.76 (0.59–0.98)
Rejected care	8.7	9.9	0.87 (0.68–1.10)	0.80 (0.62–1.03)

N = 9,543
Percentages presented.
CI: confidence interval; **OR:** odds ratio
[a] Adjusted for all variables listed in Table 4-1.
[b] Includes private home/apartment, board/care, assisted living, and group home.
[c] Includes other nursing home, psychiatric hospital, inpatient rehabilitation facility, mental retardation/developmental disabilities facility, hospice, and other.
[d] Includes Asian, Native Hawaiian/Pacific Islander, Native American/Alaska Native, and multiracial.
[e] Based on scores from 4 to 18: Resource Utilization Groups-III Activities of Daily Living score of 14 to 16 for moderate impairment, 17 or 18 for severe impairment.[46]
[f] Based on 4-level Cognitive Function Scale.[47]
[g] As assessed by reside nt interview or nursing home staff observation over a 5-day period.

CHAPTER V:

FINAL SUMMARY & CONCLUSIONS

In this dissertation, we 1) examined the quality of pain management among cancer patients residing in nursing homes (**Chapter II**); 2) explored the immediate and short-term impacts of the Medicare Part D prescription drug benefit on access to opioid analgesia among this population (**Chapter III**); and 3) examined the use of more potent opioid formulations five years after the implementation of Medicare Part D (**Chapter IV**).

5.1 Chapter II: Pain Management in Nursing Home Residents with Cancer

In **Chapter II**, we examined the use of analgesics among more than 8,000 cancer patients residing in US nursing homes in 2006 and 2007. Specifically, we estimated the prevalence and resident-level correlates of pain and receipt of analgesics among newly-admitted older and disabled nursing home residents with cancer.

We found that the majority (65.6%) of nursing home residents with a cancer diagnosis experience pain. A substantial proportion of that pain is daily, and moderate to severe in intensity. Between 2006 and 2007, 17.6% of nursing home residents whose pain occurred on a daily basis failed to receive treatment with analgesic medications in the first week of nursing home admission. These results are only modestly decreased from estimates published in 1998, prior to national efforts to improve the quality of pain management in nursing homes.

This study contributes a much-needed update to what is known about the quality of pain management in nursing home residents with cancer, a critical public health issue of increasing prominence. Pain remains common and undertreated among some of the

most vulnerable cancer patients in the US, and special attention should be paid to the oldest old, those with cognitive impairment, and residents of potentially poor quality nursing homes. Among nursing home residents overall, recent national goals for prevalence of moderate-to-severe pain were 15% for short-stay, post-acute residents and 4% for long-stay residents.[49] Although cancer-specific targets for pain management do not currently exist, these data suggest that the current state of pain management among nursing home residents with cancer falls short of these goals. New information provided in this dissertation may provide initial directions for targeted efforts to improve the quality of pain treatment in nursing homes, including redoubled efforts to disseminate older adult-specific clinical practice guidelines in this setting.

5.2 Chapter III: Should Opioid Pain Medications Receive Special Medicare Part D Coverage Protection for Nursing Home Residents with Cancer?

In **Chapter III**, we examined the relationship between the implementation of Medicare Part D and changes in fentanyl patch use among more than 18,500 nursing home residents with cancer. Given the safety and cost-related concerns surrounding the use of this potent opioid analgesic, we hypothesized that Medicare Part D led to an immediate reduction in use of fentanyl patches. To assess potential substitution, we also evaluated concomitant changes in use of similarly strong oral opioid formulations and use of less potent opioids.

We found that Medicare Part D may have had unintended effects on opioid use among nursing home residents with cancer who experienced pain. Immediately following

implementation of Medicare Part D, there were reductions in the prevalence rates of fentanyl patch and other strong opioid use and the rates of therapy days covered for all opioids. During the 18 months subsequent to Medicare Part D implementation, there were continued decreases in fentanyl patch use. These data support the notion that potential substitutions with other strong opioids and less potent opioids occurred, and suggest that the impact of Medicare Part D extended beyond the drugs and drug classes that the Medicare program explicitly excludes from coverage.

This study highlights the need for careful measurement and continual assessment of both intended and unintended effects of large-scale health policies. The immediate and continued reductions in use of fentanyl patches among nursing home residents with cancer occurred despite secular trends that may have otherwise increased access to these medications and pain management safeguards in the nursing home setting. The clinical impact of these interruptions is uncertain, and it was beyond the scope of this study to quantify the impact of Medicare Part D on quality of life among nursing home residents with cancer. In light of these patients' residence in a medically supervised setting and consequent low potential for medication abuse, expansion of Medicare Part D's coverage of pain medication and alternative opioid formulations should be considered for this vulnerable population.

5.3 Chapter IV: Naïve Initiation of Long-Acting Opioids in Nursing Home Residents

In light of evidence of interruptions in medication use patterns immediately following the implementation of Medicare Part D, we examined in **Chapter IV** the current use of long-acting opioid analgesia in the nursing home setting. Specifically, we estimated the prevalence and identified correlates of naïve-initiation of long-acting opioids among a general population of more than 9,000 Medicare beneficiaries residing in US nursing homes in 2011.

Despite known health risks associated with use of long-acting opioids to treat opioid-naïve individuals, we found that 10.0% of nursing home residents who received a long-acting opioid in the first month of a nursing home stay were not already tolerant to opioid analgesics. Individual-level factors associated with increased odds of naïve initiation of a long-acting opioid included a cancer diagnosis, terminal prognosis, functional impairment, and use of a feeding tube. Although such care is not concordant with clinical practice guidelines and FDA guidance on stepped therapy approaches, these results are significantly decreased from estimates obtained prior to large-scale changes to analgesic medication use in the nursing home setting and national efforts to heighten prescriber, patient, and caregiver awareness of safe long-acting opioid use.

5.4 Future Directions

Despite the presence of clinical practice guidelines for pain management of older adults and, more specifically, adults with cancer, this dissertation demonstrates the need

to improve the quality of pain management in the nursing home setting. Re-doubled efforts are needed to disseminate these clinical practice guidelines, improve their uptake and adoption in the long-term care setting, and make necessary adjustments to more appropriately meet the specialized needs of patients within this context.

Improvements are continually being made to the instruments that assess the medical needs of nursing home residents and the quality of their care. The replacement of MDS 2.0 with MDS 3.0 allows for greater input from the nursing home resident; therefore, future research should include re-evaluations of the prevalence of pain among nursing home residents with cancer.

In addition, prescription drug policies that are evolving at the national level may have great impact on patterns to medication use in the long-term care setting. These changes include tightening or easing of Medicare Part D formulary requirements, the number of private drug plans that participate in the prescription drug program, and the ways in which utilization requirements are employed. Moreover, the July 2012 approval of the FDA's class-wide REMS for extended-release and long-acting opioids may greatly improve education of health care providers and patients on appropriate prescribing and safe use of these potent medications. Given the challenges associated with implementation of clinical practice guidelines for pain management in nursing homes, the extent to which changes in medication safety strategies reach healthcare providers in this setting should be examined. Therefore, there is a critical need for continual evaluations of the landscape of opioid prescribing in the nursing home setting.

APPENDICES

SUPPLEMENTARY TABLES FOR CHAPTER II: PAIN MANAGEMENT IN NURSING HOME RESIDENTS WITH CANCER

Table A-1: Correlates of Pain in Older Nursing Home Residents with Cancer and Admission from a Hospital

	Pain frequency			Daily pain vs. no pain (referent)		< Daily pain vs. no pain (referent)	
	Daily n = 2,216	< Daily n = 2,538	None n = 1,856	Unadjusted OR (95% CI)	Adjusted[a] OR (95% CI)	Unadjusted OR (95% CI)	Adjusted[a] OR (95% CI)
Age, years							
65–74	18.4	22.3	28.8	Referent	Referent	Referent	Referent
75–84	45.3	45.7	45.9	0.65 (0.55–0.76)	0.68 (0.58–0.80)	0.83 (0.72–0.96)	0.84 (0.73–0.97)
≥85	36.4	32.0	25.3	0.44 (0.37–0.53)	0.47 (0.39–0.57)	0.73 (0.62–0.85)	0.73 (0.61–0.87)
Women	45.9	54.3	59.3	1.72 (1.51–1.96)	1.66 (1.44–1.93)	1.40 (1.25–1.57)	1.36 (1.19–1.54)
Race and ethnicity							
Non-Hispanic white	81.3	84.1	84.8	Referent	Referent	Referent	Referent
Non-Hispanic black	12.3	9.7	9.5	0.75 (0.61–0.91)	0.76 (0.62–0.94)	0.77 (0.62–0.95)	0.80 (0.64–1.00)
Other[b]	6.4	6.2	5.7	0.86 (0.66–1.11)	0.92 (0.70–1.20)	0.93 (0.72–1.21)	0.99 (0.76–1.28)
Widowed	43.9	46.4	44.7	1.03 (0.91–1.17)	1.00 (0.86–1.16)	1.11 (0.99–1.24)	1.06 (0.93–1.20)
Functional impairment[c]	74.8	76.0	77.5	1.16 (0.99–1.36)	1.29 (1.09–1.53)	1.07 (0.92–1.23)	1.12 (0.96–1.30)
Cognitive impairment[d]	50.8	43.5	36.5	0.56 (0.49–0.64)	0.71 (0.61–0.82)	0.75 (0.66–0.84)	0.84 (0.73–0.97)
Depressed mood[e]	5.3	6.5	11.0	2.22 (1.73–2.83)	2.18 (1.68–2.82)	1.26 (0.97–1.63)	1.21 (0.93–1.56)
Feeding tubes	7.4	7.7	5.1	0.67 (0.52–0.87)	0.70 (0.53–0.92)	1.05 (0.84–1.30)	1.11 (0.89–1.40)
Indwelling catheter	21.2	25.5	28.6	1.49 (1.29–1.72)	1.50 (1.29–1.75)	1.27 (1.12–1.46)	1.28 (1.11–1.47)
Use of restraints[f]	2.5	1.7	0.8	0.31 (0.18–0.55)	0.47 (0.26–0.85)	0.65 (0.44–0.96)	0.82 (0.55–1.23)
Bedfast	3.0	4.3	6.5	2.22 (1.61–3.06)	2.14 (1.52–3.01)	1.45 (1.05–2.01)	1.48 (1.05–2.07)
Terminal prognosis[g]	4.6	5.7	9.1	2.08 (1.59–2.70)	2.00 (1.50–2.67)	1.26 (0.97–1.63)	1.27 (0.97–1.67)

N = 6,610
CI: confidence interval; **OR:** odds ratio
[a] Adjusted for all listed variables and variables describing participation in MDS assessment (resident, family, significant other) and communication skills.
[b] Includes Hispanic, Asian or Pacific Islander, and American Indian or Alaskan Native.
[c] Activities of Daily Living Hierarchy Scale scores equal 3 or more.[41]
[d] Cognitive Performance Scale scores equal 2 or more.[43]
[e] Depression Rating Scale scores equal 3 or more.
[f] Includes trunk and limb restraints as well as chairs to prevent rising.
[g] Indicated by prognosis of <6 months or receipt of hospice.

Table A-2: Correlates of Receiving Any Analgesic in Older Nursing Home Residents with Cancer, Admission from a Hospital, and Any Pain

	Any analgesic n = 3,188	No analgesic n = 1,206	Likelihood of receiving any analgesic for any pain	
			Unadjusted OR (95% CI)	Adjusted[a] OR (95% CI)
Age, years				
65–74	26.8	20.6	Referent	Referent
75–84	46.6	43.6	0.82 (0.68–0.98)	0.88 (0.73–1.07)
≥85	26.6	35.8	0.57 (0.47–0.69)	0.67 (0.54–0.82)
Women	57.3	54.0	1.14 (0.99–1.32)	1.17 (1.00–1.37)
Race and ethnicity				
Non-Hispanic White	84.9	83.0	Referent	Referent
Non-Hispanic black	9.3	10.6	0.86 (0.69–1.06)	0.93 (0.74–1.17)
Other[b]	5.8	6.4	0.89 (0.69–1.16)	0.89 (0.67–1.18)
# other medication in first week				
≤5	24.8	44.1	Referent	Referent
6–10	40.7	33.6	2.15 (1.81–2.55)	2.33 (1.95–2.77)
≥11	34.4	22.3	2.74 (2.27–3.32)	3.02 (2.46–3.70)
Functional impairment[c]	76.6	76.9	0.98 (0.83–1.16)	1.14 (0.95–1.36)
Cognitive impairment[d]	37.1	49.8	0.59 (0.52–0.68)	0.68 (0.58–0.81)
Depressed mood[e]	8.7	7.6	1.16 (0.89–1.50)	1.14 (0.87–1.50)
Feeding tubes	6.1	8.0	0.74 (0.58–0.94)	0.69 (0.53–0.90)
Use of restraints[f]	0.9	2.3	0.39 (0.24–0.63)	0.48 (0.29–0.80)
Bedfast	5.4	4.7	1.16 (0.84–1.60)	1.17 (0.84–1.63)
Terminal prognosis[g]	7.8	5.6	1.43 (1.07–1.90)	1.66 (1.23–2.23)

N = 4,394
Percentages presented.
CI: confidence interval; **OR:** odds ratio
[a] Adjusted for all variables listed in Table A-1and variables describing participation in MDS assessment (family, significant other) and communication skills.
[b] Includes Hispanic, Asian or Pacific Islander, or American Indian or Alaskan Native.
[c] Activities of Daily Living Hierarchy Scale scores equal 3 or more.[41]
[d] Cognitive Performance Scale scores equal 2 or more.[43]
[e] Depression Rating Scale scores equal 3 or more.[42]
[f] Includes trunk and limb restraints as well as chairs to prevent rising.
[g] Indicated by prognosis of <6 months or receipt of hospice.

Table A-3: Correlates of Receiving Opioid Analgesia in Newly Admitted Nursing Home Residents with Cancer and Moderate/Severe Pain

	Opioid analgesic n = 970	No opioid analgesic n = 3,003	Likelihood of receiving an opioid for moderate/severe pain	
			Unadjusted OR (95% CI)	Adjusted[a] OR (95% CI)
Age, years				
<65	7.3	4.2	1.30 (0.90–1.89)	1.23 (0.84–1.82)
65–74	25.6	19.3	Referent	Referent
75–84	43.3	42.8	0.76 (0.63–0.93)	0.83 (0.68–1.01)
≥85	23.8	33.7	0.53 (0.43 –0.65)	0.64 (0.51–0.80)
Women	57.8	57.6	1.01 (0.87–1.16)	1.03 (0.87–1.21)
Race and ethnicity				
Non-Hispanic white	83.9	82.7	Referent	Referent
Non-Hispanic black	10.0	10.8	0.91 (0.72–1.15)	0.88 (0.68–1.14)
Other[b]	6.1	6.5	0.93 (0.69–1.25)	0.77 (0.56–1.06)
Admitted from acute hospital	89.5	85.2	1.49 (1.21–1.85)	1.42 (1.13–1.79)
# other medication in first week				
≤5	25.5	46.2	Referent	Referent
6–10	40.5	30.9	2.46 (2.07–2.93)	2.70 (2.25–3.23)
≥11	34.0	22.9	2.79 (2.31–3.36)	3.08 (2.51–3.79)
Functional impairment[c]	75.9	76.8	0.95 (0.81–1.13)	1.09 (0.90–1.32)
Cognitive impairment[d]	35.6	47.7	0.61 (0.52–0.70)	0.67 (0.56–0.80)
Depressed mood[e]	10.7	10.2	1.05 (0.83–1.33)	1.16 (0.90–1.49)
Feeding tubes	6.1	7.3	0.82 (0.62–1.09)	0.71 (0.52–0.97)
Use of restraints[f]	0.9	1.6	0.60 (0.32–1.13)	0.72 (0.38–1.36)
Bedfast	6.5	5.7	1.16 (0.85–1.57)	1.21 (0.86–1.69)
Terminal prognosis[g]	10.9	9.7	1.13 (0.89–1.45)	1.46 (1.11–1.91)

N = 3,973
Percentages presented.
CI: confidence interval; **OR:** odds ratio
[a] Adjusted for all variables listed in Table A-1 and variables describing participation in Minimum Data Set assessment (family, significant other) and communication skills.
[b] Includes Hispanic, Asian or Pacific Islander, or American Indian or Alaskan Native.
[c] Activities of Daily Living Hierarchy Scale scores equal 3 or more.[41]
[d] Cognitive Performance Scale scores equal 2 or more.[43]
[e] Depression Rating Scale scores equal 3 or more.[42]
[f] Includes trunk and limb restraints as well as chairs to prevent rising.
[g] Indicated by prognosis of <6 months or receipt of hospice

APPENDICES FOR CHAPTER III: SHOULD OPIOID PAIN MEDICATIONS RECEIVE SPECIAL MEDICARE PART D COVERAGE PROTECTION FOR NURSING HOME RESIDENTS WITH CANCER?

Table A-4: Impact of Medicare Part D on Rate of Opioid Receipt in Dual-Eligible Nursing Home Residents with Cancer, Jan 2005–Jun 2007

	WHO level 3 drugs						WHO level 2 drugs	
	All		Fentanyl patch		Other WHO level 3 drugs			
	IRR[a]	95% CI	IRR[a]	95% CI	IRR[a]	95% CI	IRR[a]	95% CI
Pre-Part D Slope	1.01	1.01–1.02	1.03	1.02–1.03	1.01	1.00–1.01	1.03	1.02–1.04
Post-Part D Slope	1.01	1.01–1.01	1.01	1.01–1.02	1.01	1.00–1.01	1.01	1.00–1.02
Change in rate in February 2006	0.89	0.86–0.92	0.88	0.83–0.93	0.90	0.84–0.96	1.03	0.95–1.13
Change in slope (after vs before Part D)	1.00	0.99–1.00	0.99	0.98–1.00	1.00	0.99–1.01	0.98	0.97–1.00

N = 4,266
CI: confidence interval; **IRR:** incidence rate ratio
[a] Adjusted for serial correlation using Newey-West standard errors

APPENDICES FOR CHAPTER IV: NAÏVE INITIATION OF LONG-ACTING OPIOIDS IN NURSING HOME RESIDENTS

Table A-5: Correlates of Naive Long-Acting Opioid Initiation in Nursing Home Residents with Cancer

	Naïve initiation (n = 244)	Non-naïve initiation (n = 1,416)	Likelihood of naïve initiation	
			Unadjusted OR (95% CI)	Adjusted[a] OR (95% CI)
Source of admission				
Acute hospital	56.2	60.2	0.92 (0.66–1.27)	0.85 (0.60–1.20)
Community[b]	26.2	25.8	Referent	Referent
Other[c]	17.6	14.1	1.23 (0.79–1.93)	1.23 (0.78–1.94)
Age, years				
<65	15.6	14.8	1.12 (0.72–1.74)	1.17(0.75–1.82)
65–74	28.3	30.1	Referent	Referent
75–84	36.1	32.1	1.19 (0.85–1.67)	1.21 (0.86–1.71)
≥85	20.1	23.0	0.93 (0.63–1.37)	0.94 (0.61–1.44)
Women	61.9	63.4	0.94 (0.71–1.25)	1.00 (0.74–1.34)
Race and ethnicity				
Non-Hispanic white	83.2	82.6	Referent	Referent
Non-Hispanic black	10.7	10.6	1.00 (0.63–1.58)	0.97 (0.61–1.56)
Hispanic or Latino	4.1	4.3	0.94 (0.47–1.89)	0.88 (0.43–1.80)
Other[d]	2.1	2.5	0.80 (0.31–2.07)	0.80 (0.29–2.23)
Life expectancy of <6 months	36.9	24.9	1.77 (1.33–2.35)	1.66 (1.23–2.24)
Moderate/severe functional impairment[e]	75.0	67.6	1.44 (1.07–1.94)	1.45 (1.06–1.99)
Moderate/severe cognitive impairment[f]	52.1	46.5	1.26 (0.94–1.70)	1.14(0.81–1.59)
Parenteral feeding or feeding tube	7.4	5.6	1.35 (0.80–2.27)	1.49 (0.86–2.59)
Difficulty chewing	3.3	2.9	1.14 (0.53–2.46)	1.09 (0.50–2.37)
Difficulty swallowing	7.0	8.3	0.82 (0.48–1.40)	0.76 (0.43–1.32)
Clinical conditions				

	Naïve initiation (n = 244)	Non-naïve initiation (n = 1,416)	Likelihood of naïve initiation	
			Unadjusted OR (95% CI)	Adjusted[a] OR (95% CI)
Arthritis	20.5	26.3	0.72 (0.52–1.00)	0.78 (0.55–1.10)
Osteoporosis	6.6	11.9	0.52 (0.30–0.88)	0.54 (0.31–0.94)
Hip fracture	6.2	3.4	1.87 (1.03–3.38)	2.07 (1.12–3.82)
Asthma, chronic obstructive pulmonary disease, or chronic lung disease	27.5	29.8	0.89 (0.66–1.20)	0.95 (0.70–1.29)
Respiratory failure	1.2	1.3	0.92 (0.27–3.09)	0.80 (0.22–2.92)
Heart failure	13.9	14.1	0.99 (0.67–1.47)	1.09 (0.73–1.64)
Alzheimer disease	2.9	2.2	1.32 (0.57–3.04)	1.64 (0.67–4.06)
Stroke	4.5	6.6	0.66 (0.35–1.26)	0.70 (0.37–1.35)
Rejected care	9.0	10.2	0.88 (0.54–1.41)	0.76 (0.45–1.27)

N = 1,660
Percentages presented.
CI: confidence interval; **OR:** odds ratio
[a] Adjusted for all listed variables.
[b] Includes private home/apartment, board/care, assisted living, and group home.
[c] Includes other nursing home, psychiatric hospital, inpatient rehabilitation facility, mental retardation/developmental disabilities facility, hospice, and other.
[d] Includes Asian, Native Hawaiian/Pacific Islander, Native American/Alaska Native, and multiracial.
[e] Based on scores from 4 to 18: Resource Utilization Groups-III Activities of Daily Living score of 14 to 16 for moderate impairment, 17 or 18 for severe impairment.[46]
[f] Based on 4-level Cognitive Function Scale.[47]
[g] As assessed by resident interview or nursing home staff observation over a 5-day period.

Table A-6: Correlates of Naive Long-Acting Opioid Initiation Anytime After Nursing Home Admission

	Naïve initiation (n = 1,262)	Non-naïve initiation (n = 8,281)	Likelihood of naïve initiation	
			Unadjusted OR (95% CI)	Adjusted[a] OR (95% CI)
Source of admission				
Acute hospital	60.4	58.0	1.33 (1.13–1.56)	1.23 (1.04–1.45)
Community[b]	19.0	24.3	Referent	Referent
Other[c]	20.6	17.7	1.48 (1.22–1.80)	1.44 (1.18–1.75)
Age, years				
<65	21.9	19.8	1.09 (0.91–1.30)	1.12 (0.93–1.34)
65–74	23.6	23.3	Referent	Referent
75–84	31.2	29.4	1.05 (0.89–1.23)	1.15 (0.97–1.36)
≥85	23.3	27.5	0.83 (0.70–0.99)	1.00 (0.83–1.20)
Women	66.6	73.1	0.73 (0.65–0.83)	0.81 (0.71–0.92)
Race and ethnicity				
Non-Hispanic white	85.3	86.6	Referent	Referent
Non-Hispanic black	9.4	7.9	1.22 (0.99–1.50)	1.07 (0.87–1.33)
Hispanic or Latino	3.3	3.9	0.86 (0.61–1.20)	0.80 (0.57–1.13)
Other[d]	1.9	1.6	1.18 (0.77–1.81)	1.08 (0.69–1.69)
Life expectancy of <6 months	13.1	7.4	1.87 (1.57–2.23)	1.57 (1.28–1.92)
Moderate/severe functional impairment[e]	74.8	70.6	1.24 (1.08–1.42)	1.24 (1.07–1.43)
Moderate/severe cognitive impairment[f]	23.1	21.4	1.10 (0.96–1.27)	1.06 (0.90–1.24)
Parenteral feeding or feeding tube	6.3	3.9	1.63 (1.27–2.09)	1.37 (1.05–1.79)
Difficulty chewing	2.5	2.1	1.15 (0.79–1.69)	1.10 (0.75–1.62)
Difficulty swallowing	5.3	5.0	1.06 (0.81–1.38)	0.90 (0.68–1.20)
Key diagnoses				
Cancer	23.4	16.5	1.55 (1.34–1.79)	1.33 (1.13–1.57)
Arthritis	32.5	37.9	0.79 (0.70–0.90)	0.89 (0.79–1.02)
Osteoporosis	14.8	19.7	0.71 (0.60–0.84)	0.83 (0.69–0.98)

	Naïve initiation (n = 1,262)	Non-naïve initiation (n = 8,281)	Likelihood of naïve initiation	
			Unadjusted OR (95% CI)	Adjusted[a] OR (95% CI)
Hip fracture	4.4	3.9	1.14 (0.85–1.54)	1.14 (0.85–1.54)
Asthma, chronic obstructive pulmonary disease, or chronic lung disease	33.5	28.9	1.24 (1.09–1.41)	1.20 (1.06–1.37)
Respiratory failure	3.0	1.8	1.66 (1.16–2.38)	1.30 (0.89–1.90)
Heart failure	20.1	18.4	1.11 (0.95–1.29)	1.10 (0.95–1.29)
Alzheimer disease	3.6	4.8	0.74 (0.54–1.00)	0.83 (0.60–1.15)
Stroke	8.3	9.1	0.90 (0.73–1.12)	0.87 (0.70–1.08)
Rejected care	8.9	10.0	0.88 (0.72–1.09)	0.84 (0.67–1.04)

N = 9,543

Percentages presented.

CI: confidence interval; **OR:** odds ratio

[a] Adjusted for all listed variables.

[b] Includes private home/apartment, board/care, assisted living, and group home.

[c] Includes other nursing home, psychiatric hospital, inpatient rehabilitation facility, mental retardation/developmental disabilities facility, hospice, and other.

[d] Includes Asian, Native Hawaiian/Pacific Islander, Native American/Alaska Native, and multiracial.

[e] Based on scores from 4 to 18: Resource Utilization Groups-III Activities of Daily Living score of 14 to 16 for moderate impairment, 17 or 18 for severe impairment.[46]

[f] Based on 4-level Cognitive Function Scale.[47]

[g] As assessed by resident interview or nursing home staff observation over a 5-day period.

Table A-7: Correlates of Naive Long-Acting Opioid Initiation (90-Day Look Back Period)

	Naïve initiation (n = 602)	Non-naïve initiation (n = 8,941)	Likelihood of naïve initiation	
			Unadjusted OR (95% CI)	Adjusted[a] OR (95% CI)
Source of admission				
Acute hospital	58.5	58.3	1.29 (1.03–1.61)	1.26 (1.00–1.58)
Community[b]	18.6	23.9	Referent	Referent
Other[c]	22.9	17.8	1.66 (1.26–2.18)	1.68 (1.27–2.22)
Age				
<65	19.3	20.1	0.98 (0.76–1.26)	1.03 (0.80–1.34)
65–74	22.9	23.3	Referent	Referent
75–84	32.9	29.5	1.14 (0.91–1.42)	1.22 (0.97–1.53)
≥85	24.9	27.1	0.94 (0.74–1.19)	1.07 (0.83–1.37)
Women	67.6	72.6	0.79 (0.66–0.94)	0.86 (0.71–1.03)
Race and ethnicity				
Non-Hispanic white	85.2	86.5	Referent	Referent
Non-Hispanic black	10.0	7.9	1.27 (0.96–1.68)	1.17 (0.88–1.57)
Hispanic or Latino	3.0	3.9	0.78 (0.47–1.27)	0.72 (0.43–1.20)
Other[d]	1.8	1.7	1.12 (0.61–2.06)	1.01 (0.53–1.91)
Life expectancy of <6 months	18.6	7.5	2.83 (2.29–3.50)	2.30 (1.81–2.93)
Moderate/severe functional impairment[e]	77.6	70.7	1.43 (1.18–1.74)	1.39 (1.13–1.70)
Moderate/severe cognitive impairment[f]	26.4	21.3	1.33 (1.11–1.60)	1.15 (0.93–1.42)
Parenteral feeding or feeding tube	5.7	4.2	1.38 (0.97–1.98)	1.16 (0.78–1.70)
Difficulty chewing	1.8	2.2	0.83 (0.45–1.52)	0.75 (0.40–1.41)
Difficulty swallowing	5.7	5.0	1.13 (0.79–1.61)	0.94 (0.65–1.36)
Key diagnoses				
Cancer	26.4	16.8	1.78 (1.46–2.16)	1.36 (1.10–1.70)
Arthritis	29.7	37.6	0.70 (0.58–0.84)	0.78 (0.65–0.95)
Osteoporosis	15.5	19.3	0.77 (0.61–0.96)	0.91 (0.72–1.15)
Hip fracture	4.3	4.0	1.10 (0.73–1.64)	1.06 (0.70–1.59)

	Naïve initiation (n = 602)	Non-naïve initiation (n = 8,941)	Likelihood of naïve initiation	
			Unadjusted OR (95% CI)	Adjusted[a] OR (95% CI)
Asthma, chronic obstructive pulmonary disease, or chronic lung disease	31.6	29.4	1.11 (0.93–1.33)	1.10 (0.91–1.33)
Respiratory failure	2.5	2.0	1.28 (0.75–2.18)	1.11 (0.64–1.95)
Heart failure	20.3	18.5	1.12 (0.90–1.38)	1.11 (0.89–1.38)
Alzheimer disease	3.8	4.7	0.81 (0.53–1.24)	0.85 (0.55–1.32)
Stroke	7.8	9.1	0.85 (0.63–1.14)	0.81 (0.60–1.10)
Rejected care	8.5	9.9	0.84 (0.62–1.14)	0.76 (0.55–1.04)

N = 9,543
Percentages presented.
CI: confidence interval; **OR:** odds ratio
[a] Adjusted for all listed variables.
[b] Includes private home/apartment, board/care, assisted living, and group home.
[c] Includes other nursing home, psychiatric hospital, inpatient rehabilitation facility, mental retardation/developmental disabilities facility, hospice, other.
[d] Includes Asian, Native Hawaiian/Pacific Islander, Native American/Alaska Native, and multiracial.
[e] Based on scores from 4 to 18: Resource Utilization Groups-III Activities of Daily Living score of 14 to 16 for moderate impairment, 17 or 18 for severe impairment.[46]
[f] Based on 4-level Cognitive Function Scale.[47]
[g] As assessed by resident interview or nursing home staff observation over a 5-day period.

REFERENCES

1. American Cancer Society. Cancer Facts & Figures 2015. Atlanta, GA: American Cancer Society; 2015.

2. Howlader N, Noone AM, Krapcho M, Howlader N, Noone AM, Krapcho M, Neyman N, Aminou R, Waldron W, Altekruse SF, Kosary CL, Ruhl J, Tatalovich Z, Cho H, Mariotto A, Eisner MP, Lewis DR, Chen HS, Feuer EJ, Cronin KA (eds). SEER Cancer Statistics Review, 1975-2009 (Vintage 2009 Populations), National Cancer Institute. Bethesda, MD. http://seer.cancer.gov/csr/1975_2009_pops09/, based on November 2011 SEER data submission, posted to the SEER web site, April 2012.

3. Allcock N, McGarry J, Elkan R. Management of pain in older people within the nursing home: a preliminary study. Health Soc Care Community 2002 Nov;10(6):464-71.

4. Harrington C, Carrillo H, Dowdell M, Tang PP, Blank BW. Nursing facilities, staffing, residents and facility deficiencies, 2005 through 2010. 2011 Oct. Available at: http://www.theconsumervoice.org/sites/default/files/OSCAR-2011-final.pdf

5. Johnson VMP, Teno JM, Bourbonniere M, Mor V. Palliative care needs of cancer patients in U.S. nursing homes. J Palliat Med 2005 Apr;8(2):273-9.

6. Bernabei R, Gambassi G, Lapane K, Landi F, Gatsonis C, Dunlop R, Lipsitz L, Steel K, Mor V. Management of pain in elderly patients with cancer. SAGE Study Group. Systematic Assessment of Geriatric Drug Use via Epidemiology. JAMA 1998 Jun 17;279(23):1877-82.

7. Pergolizzi J, Böger RH, Budd K, Dahan A, Erdine S, Hans G, Kress HG, Langford R, Likar R, Raffa RB, Sacerdote P. Opioids and the management of chronic severe pain in the elderly: consensus statement of an International Expert Panel with focus on the six clinically most often used World Health Organization Step III opioids (buprenorphine, fentanyl, hydromorphone, methadone, morphine, oxycodone). Pain Pract 2008 Jul-Aug;8(4):287-313.

8. Plante GE, VanItallie TB. Opioids for cancer pain: the challenge of optimizing treatment. Metabolism 2010 Oct;59 Suppl 1:S47-52.

9. Stjernswärd J. WHO cancer pain relief programme. Cancer Surv 1988;7(1):195-208.

10. National Comprehensive Cancer Network Clinical Practice Guidelines in Oncology: Adult Cancer Pain. Available at: http://www.nccn.org/professionals/physician_gls/pdf/pain.pdf.

11. US Centers for Medicare and Medicaid Services. Medicare Prescription Drug Benefit Manual, Chapter 6 - Part D Drugs and Formulary Requirements. Available at: http://www.cms.gov/Medicare/Prescription-Drug-Coverage/PrescriptionDrugCovContra/Downloads/Chapter6.pdf.

12. Cramer GW, Galer BS, Mendelson MA, Thompson GD. A drug use evaluation of selected opioid and nonopioid analgesics in the nursing facility setting. J Am Geriatr Soc 2000 Apr;48(4):398-404.

13. Stevenson DG, Keohane LM, Mitchell SL, Zarowitz BJ, Huskamp HA. Medicare part D claims rejections for nursing home residents, 2006 to 2010. Am J Manag Care 2012 Oct;18(10):647-54.

14. US Census Bureau. State and County QuickFacts. 2015. Available at: http://quickfacts.census.gov/qfd/states/00000.html.

15. Adminstration on Aging. A Profile of Older Americans: 2011. 2011. Available at: http://www.aoa.gov/Aging_Statistics/Profile/2011/docs/2011profile.pdf.

16. Centers for Disease Control and Prevention, Office of Statistics and Programming. 10 leading causes of death by age group, United States - 2010. 2010. Available at: http://www.cdc.gov/injury/wisqars/pdf/10LCID_All_Deaths_By_Age_Group_2010-a.pdf.

17. Hodgson NA, Given CW. Determinants of functional recovery in older adults surgically treated for cancer. Cancer Nurs 2004 Jan-Feb; 27(1):10-6.

18. Rao A, Cohen HJ. Symptom management in the elderly cancer patient: fatigue, pain, and depression. J Natl Cancer Inst Monogr 2004;32:150-7.

19. van den Beuken-van Everdingen MH, de Rijke JM, Kessels AG, Schouten HC, van Kleef M, Patijn J. Prevalence of pain in patients with cancer: a systematic review of the past 40 years. Ann Oncol 2007 Sep;18(9):1437-49.

20. Tan G, Jensen MP, Thornby JI, Shanti BF. Validation of the Brief Pain Inventory for chronic nonmalignant pain. J Pain 2004 Mar;5(2):133-7.

21. de Bock GH, van Marwijk HW, Kaptein AA, Mulder JD. Osteoarthritis pain assessment in family practice. Arthritis Care Res 1994 Mar;7(1):40-5.

22. Foley KM. The relationship of pain and symptom management to patient requests for physician-assisted suicide. J Pain Symptom Manage 1991 Jul;6(5):289-97.

23. Jovey RD, Ennis J, Gardner-Nix J, Goldman B, Hays H, Lynch M, Moulin D; Canadian Pain Society. Use of opioid analgesics for the treatment of chronic noncancer pain—a consensus statement and guidelines from the Canadian Pain Society, 2002. Pain Res Manag 2003 Spring;8 Suppl A:3A-28A.

24. Zech DF, Grond S, Lynch J, Hertel D, Lehmann KA. Validation of World Health Organization Guidelines for cancer pain relief: a 10-year prospective study. Pain 1995 Oct;63(1):65-76.

25. Levy, MH. Pharmacologic treatment of cancer pain. N Engl J Med 1996 Oct 10;335(15):1124-32.

26. Liu K. A data perspective on long-term care. Gerontologist 1994 Aug;34(4):476-80.

27. Murtaugh CM, Kemper P, Spillman BC, Carlson BL. The amount, distribution, and timing of lifetime nursing home care. Med Care 1997 Mar;35(3):204-18.

28. Kemper P, Murtaugh CM. Lifetime use of nursing home care. N Engl J Med 1991 Feb 28;324(9):595-600.

29. Parry C, Kent EE, Mariotto AB, Alfano CM, Rowland JH. Cancer survivors: a booming population. Cancer Epidemiol Biomarkers Prev 2011 Oct;20(10):1996-2005.

30. Teno JM, Gozalo PL, Bynum JP. Change in end-of-life care for Medicare beneficiaries: site of death, place of care, and health care transitions in 2000, 2005, and 2009. JAMA 2013 Feb 6;309(5):470-7.

31. Rigler SK, Shireman TI, Kallenbach L. Predictors of long-acting opioid use and oral versus transdermal route among older Medicaid beneficiaries. Am J Geriatr Pharmacother 2007 Jun;5(2):91-9.

32. Dosa DM, Dore DD, Mor V, Teno JM. Frequency of long-acting opioid analgesic initiation in opioid-naïve nursing home residents. J Pain Symptom Manage 2009 Oct;38(4):515-21.

33. Monroe TB, Carter MA, Feldt KS, Dietrich MS, Cowan RL. Pain and hospice care in nursing home residents with dementia and terminal cancer. Geriatr Gerontol Int 2013 Oct;13(4):1018-25

34. Monroe T, Carter M, Feldt K, Tolley B, Cowan RL. Assessing advanced cancer pain in older adults with dementia at the end-of-life. J Adv Nurs 2012 Sep;68(9):2070-8.

35. Henry J. Kaiser Family Foundation. Distribution of certified nursing facility residents by primary payer source. 2010. Available at: http://kff.org/other/state-indicator/residents-by-primary-payer-source/.

36. United States Government Accountability Office. Instances of questionable access to prescription drugs. 2011. Available at: http://www.gao.gov/assets/590/585424.pdf.

37. Huskamp HA, Stevenson DG, Keating NL, Newhouse JP. Rejections of drug claims for nursing home residents under Medicare Part D. Health Aff (Millwood) 2008 Mar-Apr;27(2):560-7.

38. Briesacher BA, Soumerai SB, Field TS, Fouayzi H, Gurwitz JH. Medicare part D's exclusion of benzodiazepines and fracture risk in nursing homes. Arch Intern Med 2010 Apr 26;170(8):693-8.

39. Minimum Data Set Plus Training Manual. Natick, MA: Eliot Press, 1991.

40. Morris JN, Hawes C, Fries BE, Phillips CD, Mor V, Katz S, Murphy K, Drugovich ML, Friedlob AS. Designing the national resident assessment instrument for nursing homes. Gerontologist 1990 Jun;30(3):293-307.

41. Phillips CD, Morris JN, Hawes C. Association of the Resident Assessment Instrument (RAI) with changes in function, cognition, and psychosocial status. J Am Geriatr Soc 1997 Aug;45(8):986-93.

42. Burrows AB, Morris JN, Simon SE, Hirdes JP, Phillips C. Development of a minimum data set-based depression rating scale for use in nursing homes. Age Ageing 2000 Mar;29(2):165-72.

43. Morris JN, Fries BE, Mehr DR. MDS Cognitive Performance Scale. J Gerontol 1994 Jun;49(4):M174-82.

44. US Centers for Medicare and Medicaid Services. MDS 3.0 RAI Manual. 2014 October. Available at: http://www.cms.gov/Medicare/Quality-Initiatives-Patient-Assessment-Instruments/NursingHomeQualityInits/MDS30RAIManual.html.

45. Saliba D, Buchanan J. Making the investment count: revision of the Minimum Data Set for nursing homes, MDS 3.0. J Am Med Dir Assoc 2012 Sep;13(7):602-10.

46. Fries BE, Schneider DP, Foley WJ, Gavazzi M, Burke R, Cornelius E. Refining a case-mix measure for nursing homes: Resource Utilization Groups (RUG-III). Med Care 1994 Jul;32(7):668-85.

47. Thomas KS, Dosa D, Wysocki A, Mor V. The Minimum Data Set 3.0 Cognitive Function Scale. Med Care 2015 Mar, electronically published ahead of print.

48. Hawes C, Morris JN, Phillips CD, Mor V, Fries BE, Nonemaker S. Reliability estimates for the Minimum Data Set for nursing home resident assessment and care screening (MDS). Gerontologist 1995 Aug;35(2):172-8.

49. World Health Organization. Cancer Pain Relief: With a Guide to Opioid Availability, 2nd ed. Geneva, Switzerland: World Health Organization; 1996.

50. Practice guidelines for cancer pain management. A report by the American Society of Anesthesiologists Task Force on Pain Management, Cancer Pain Section. Anesthesiology. 1996 May;84(5):1243-57.

51. Ripamonti CI, Santini D, Maranzano E, Berti M, Roila F; ESMO Guidelines Working Group. Management of cancer pain: ESMO Clinical Practice Guidelines. Ann Oncol. 2012 Oct;23 Suppl 7:vii139-54.

52. Argoff CE, Silvershein DI. A comparison of long- and short-acting opioids for the treatment of chronic noncancer pain: tailoring therapy to meet patient needs. Mayo Clin Proc 2009 Jul;84(7):602-12.

53. Hardin JW, Hilbe JM. Generalized Estimating Equations, 2nd ed. Boca Raton, FL: CRC Press, 2013.

54. Hosmer D, Lemeshow S. Applied Logistic Regression. New York, NY: John Wiley & Sons, 2000.

55. Wagner AK, Soumerai SB, Zhang F, Ross-Degnan D. Segmented regression analysis of interrupted time series studies in medication use research. J Clin Pharm Ther 2002 Aug;27(4):299-309.

56. Piza EL. Using Poisson and Negative Binomial Regression Models to Measure the Influence of Risk on Crime Incident Counts. Available at: http://rutgerscps.weebly.com/uploads/2/7/3/7/27370595/countregressionmodels.pdf.

57. Ostrom C. Time series analysis. In: Sage University Papers Series on Quantitative Applications in the Social Sciences. Thousand Oaks, CA: Sage Publications, Inc., 1990.

58. Durbin J, Watson G. Testing for serial correlation in least square regression. Biometrika 1951;37:409-428.

59. Newey WK, West KD. Automatic lag selection in covariance matrix estimation. Rev Econ Stud 1994;61(4):631-53.

60. Harris Y, Clauser SB. Achieving improvement through nursing home quality measurement. Health Care Financ Rev 2002 Summer;23(4):5-18.

61. Rollow W, Lied TR, McGann P, Poyer J, LaVoie L, Kambic RT, Bratzler DW, Ma A, Huff ED, Ramunno LD. Assessment of the Medicare quality improvement organization program. Ann Intern Med 2006 Sep;145(5):342-53.

62. Teno J, Bird C, Mor V. The Prevalence and Treatment of Pain in U.S. Nursing Homes. Providence RI, 1999.

63. Edelen MO, Saliba D. Correspondence of verbal descriptor and numeric rating scales for pain intensity: an item response theory calibration. J Gerontol A Biol Sci Med Sci 2010 Jul;65(7):778-85.

64. Lanser P, Gesell S. Pain management: the fifth vital sign. Healthc Benchmarks 2001;8(6):68-70, 62.

65. Morris JN, Murphy K, Nonemaker S. Long-Term Care Facility Resident Assessment (RAI) User's Manual, October 2005. Available at www.cms.gov/Medicare/Quality-Initiatives-Patient-Assessment-Instruments/NursingHomeQualityInits/NHQIMDS20.html.

66. Morris JN, Fries BE, Morris SA. Scaling ADLs within the MDS. J Gerontol A Biol Sci Med Sci 1999 Nov;54(11):M546–53.

67. Fries BE, Simon SE, Morris JN, Flodstrom C, Bookstein FL. Pain in U.S. nursing homes: Validating a pain scale for the Minimum Data Set. Gerontologist 2001 Apr;41(2):173–9.

68. American Geriatrics Society Panel on Pharmacological Management of Persistent Pain in Older Persons. Pharmacological management of persistent pain in older persons. J Am Geriatr Soc 2009 Aug;57(8):1331-46.

69. Rogers WH. Regression standard errors in clustered samples. Stata Tech Bull 1993;3(13):19-23.

70. Berg K, Mor V, Morris J, Murphy KM, Moore T, Harris Y. Identification and evaluation of existing nursing homes quality indicators. Health Care Financ Rev 2002 Summer;23(4):19-36.

71. University of Wisconsin-Madison Pain & Policy Studies Group. Database of Statutes, Regulations, & Other Policies for Pain Management. Available at www.painpolicy.wisc.edu/database-statutes-regulations-otherpolicies-pain-management.

72. Federation of State Medical Boards. Model Policy on the Use of Opioid Analgesics in the Treatment of Chronic Pain, July 2013. Available at www.fsmb.org/pdf/pain_policy_july2013.pdf.

73. Cleeland CS, Gonin R, Hatfield AK, Edmonson JH, Blum RH, Stewart JA, Pandya KJ. Pain and its treatment in outpatients with metastatic cancer. N Engl J Med 1994 Mar 3;330(9):592–6.

74. Schafheutle EI, Cantrill JA, Noyce PR. Why is pain management suboptimal on surgical wards? J Adv Nurs 2001 Mar;33(6):728–37.

75. Clement JP, Bradley CJ, Lin C. Organizational characteristics and cancer care for nursing home residents. Health Serv Res 2009 Dec;44(6):1983–2003.

76. Grabowski DC, Gruber J, Angelelli JJ. Nursing home quality as a common good. Rev Econ Stat 2008 Nov 1;90(4):754–64.

77. Castle NG. Nursing homes with persistent deficiency citations for physical restraint use. Med Care 2002 Oct;40(10):868–78.

78. Vargas-Schaffer G. Is the WHO analgesic ladder still valid? Twenty-four years of experience. Can Fam Physician 2010 Jun;56(6):514–7, e202-5.

79. Eisenberg E, Marinangeli F, Birkhahn J, Paladini A, Varrassi G. Time to modify the WHO analgesic ladder? Pain Clin Update 2005 Dec;13(5):1–4.

80. Miguel R. Interventional treatment of cancer pain: The fourth step in the World Health Organization analgesic ladder? Cancer Control 2000 Mar-Apr;7(2):149–56.

81. Jadad AR, Browman GP. The WHO analgesic ladder for cancer pain management. JAMA 1995 Dec 20;274(23):1870–3.

82. Advancing Excellence in America's Nursing Homes. Nursing Home Quality Improvement Campaign Announces Progress on Clinical Goals, September 2008.

Available at
www.michigan.gov/documents/mdch/CampaignResultsSummary_256377_7.pdf.

83. Chen Y-C, Kreling DH. The effect of the Medicare Part D benzodiazepine exclusion on the utilization patterns of benzodiazepines and substitute medications. Res Social Adm Pharm 2014 Mar-Apr;10(2):438-47.

84. Ong MK, Zhang L, Xu H, Azocar F, Ettner SL. Medicare Part D benzodiazepine exclusion and use of psychotropic medication by patients with new anxiety disorders. Psychiatr Serv 2012 Jul;63(7):637-42.

85. Ong MK, Xu H, Zhang L, Azocar F, Ettner SL. Effect of medicare part D benzodiazepine exclusion on psychotropic use in benzodiazepine users. J Am Geriatr Soc 2012 Jul;60(7):1292-7.

86. Huskamp HA, Stevenson DG, O'Malley AJ, Dusetzina SB, Mitchell SL, Zarowitz BJ, Chernew ME, Newhouse JP. Medicare Part D plan generosity and medication use among dual-eligible nursing home residents. Med Care 2013 Oct;51(10):894-900.

87. US Food and Drug Administration. FDA Public Health Advisory: Important Information for the Safe Use of Fentanyl Transdermal System (Patch). 2007 December 21. Available at: http://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/ucm051257.htm.

88. Mercadante S, Arcuri E. Pharmacological management of cancer pain in the elderly. Drugs Aging 2007;24(9):761-76.

89. Pimentel CB, Briesacher BA, Gurwitz JH, Rosen AB, Pimentel MT, Lapane KL. Pain management in nursing home residents with cancer. J Am Geriatr Soc 2015 Apr;63(4):633–41.

90. Fentanyl Prices, Coupons and Patient Assistance Programs. 2015. Available at: http://www.drugs.com/price-guide/fentanyl.

91. Omnibus Budget Reconciliation Act of 1987, Pub. L. No. 100-203, Subtitle C: Nursing Home Reform (1987).

92. Briesacher BA, Soumerai SB, Field TS, Fouayzi H, Gurwitz JH. Nursing home residents and enrollment in Medicare Part D. J Am Geriatr Soc 2009 Oct;57(10):1902-7.

93. Stevenson DG, Huskamp HA, Keating NL, Newhouse JP. Medicare Part D and nursing home residents. J Am Geriatr Soc 2007 Jul;55(7):1115-25.

94. Skaer TL. Practice guidelines for transdermal opioids in malignant pain. Drugs 2004;64(23):2629-38.

95. Institute of Medicine Committee on Approaching Death: Addressing Key End of Life Issues. Dying in America: Improving Quality and Honoring Individual Preferences Near the End of Life. Washington, DC: The National Academies Press; 2014.

96. Gurwitz JH, Field TS, Judge J, Rochon P, Harrold LR, Cadoret C, Lee M, White K, LaPrino J, Erramuspe-Mainard J, DeFlorio M, Gavendo L, Auger J, Bates DW. The incidence of adverse drug events in two large academic long-term care facilities. Am J Med 2005 Mar;118(3):251-8.

97. US Food and Drug Administration. Safety Warnings Regarding Use of Fentanyl Transdermal (Skin) Patches. 2005 July 7. Available at: http://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/ucm051739.htm.

98. Dorsey ER, Rabbani A, Gallagher SA, Conti RM, Alexander GC. Impact of FDA black box advisory on antipsychotic medication use. Arch Intern Med 2010 Jan;170(1):96-103.

99. Hartung DM, Middleton L, Markwardt S, Williamson K, Ketchum K. Changes in long-acting β-agonist utilization after the FDA's 2010 drug safety communication. Clin Ther 2015 Jan;37(1):114-23.

100. Valluri S, Zito JM, Safer DJ, Zuckerman IH, Mullins CD, Korelitz JJ. Impact of the 2004 Food and Drug Administration pediatric suicidality warning on antidepressant and psychotherapy treatment for new-onset depression. Med Care 2010 Nov;48(11):947-54.

101. Aspinall SE, Zhao X, Good CB, Stone RA, Smith KJ, Cunningham FE. FDA warning and removal of rosiglitazone from VA national formulary. Am J Manag Care 2013 Sep;19(9):748-58.

102. Shah ND, Montori VM, Krumholz HM, Tu K, Alexander GC, Jackevicius CA. Responding to an FDA warning--geographic variation in the use of rosiglitazone. N Engl J Med 2010 Nov;363(22):2081-4.

103. Cohen A, Rabbani A, Shah N, Alexander GC. Changes in glitazone use among office-based physicians in the U.S., 2003-2009. Diabetes Care 2010 Apr;33(4):823-5.

104. Mor V, Intrator O, Unruh MA, Cai S. Temporal and Geographic variation in the validity and internal consistency of the Nursing Home Resident Assessment Minimum Data Set 2.0. BMC Health Serv Res 2011 Apr;11:78.

105. US Centers for Medicare and Medicaid Services. Design for Nursing Home Compare Five-Star Quality Rating System: Technical Users' Guide. 2015. Available at: http://www.cms.gov/Medicare/Provider-Enrollment-and-Certification/CertificationandComplianc/Downloads/usersguide.pdf.

106. US Department of Justice. Practitioner's Manual: An Informational Outline of the Controlled Substances Act. 2006. Available at: http://www.deadiversion.usdoj.gov/pubs/manuals/pract/pract_manual012508.pdf.

107. Lapane KL, Quilliam BJ, Chow W, Kim MS. Impact of revisions to the F-Tag 309 surveyors' interpretive guidelines on pain management among nursing home residents. Drugs Aging 2012 May;29(5):385-93.

108. Koh NY, Koo WH. Polypharmacy in palliative care: can it be reduced? Singapore Med J 2002 Jun;43(6):279-83.

109. Riechelmann RP, Krzyzanowska MK, O'Carroll A, Zimmermann C. Symptom and medication profiles among cancer patients attending a palliative care clinic. Support Care Cancer 2007 Dec;15(12):1407-12.

110. Currow DC, Stevenson JP, Abernethy AP, Plummer J, Shelby-James TM. Prescribing in palliative care as death approaches. J Am Geriatr Soc. 2007 Apr;55(4):590-5.

111. Nauck F, Ostgathe C, Klaschik E, Bausewein C, Fuchs M, Lindena G, Neuwöhner K, Schulenberg D, Radbruch L; Working Group on the Core Documentation for Palliative Care Units in Germany. Drugs in palliative care: results from a representative survey in Germany. Palliat Med 2004 Mar;18(2):100-7.

112. US Food and Drug Administration. Extended-Release (ER) and Long-Acting (LA) Opioid Analgesic Risk Evaluation and Mitigation Strategy (REMS). 2014 Dec. Available at: http://www.fda.gov/downloads/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/UCM311290.pdf.

113. Mercadante S, Craig D, Giarratano A. US Food and Drug Administration's Risk Evaluation and Mitigation Strategy for extended-release and long-acting opioids: pros and cons, and a European perspective. Drugs 2012 Dec;72(18):2327-32.